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NEWS
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NEWS 2
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                WPIDS/WPIX enhanced with new FRAGHITSTR display format
NEWS 3
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        MAR 20 MARPAT now updated daily
NEWS 5
        MAR 22 LWPI reloaded
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NEWS 7
        APR 02 JICST-EPLUS removed from database clusters and STN
NEWS 8 APR 30 GENBANK reloaded and enhanced with Genome Project ID field
NEWS 9 APR 30 CHEMCATS enhanced with 1.2 million new records
NEWS 10 APR 30 CA/CAplus enhanced with 1870-1889 U.S. patent records
NEWS 11 APR 30 INPADOC replaced by INPADOCDB on STN
NEWS 12 MAY 01
                New CAS web site launched
NEWS 13
        MAY 08
                CA/CAplus Indian patent publication number format defined
NEWS 14 MAY 14
                RDISCLOSURE on STN Easy enhanced with new search and display
        MAY 21 BIOSIS reloaded and enhanced with archival data
NEWS 15
NEWS 16
        MAY 21
                TOXCENTER enhanced with BIOSIS reload
NEWS 17
        MAY 21
                CA/CAplus enhanced with additional kind codes for German
                patents
        MAY 22
NEWS 18
                CA/CAplus enhanced with IPC reclassification in Japanese
                patents
NEWS 19
        JUN 18 CA/CAplus to be enhanced with pre-1967 CAS Registry Numbers
NEWS EXPRESS NOVEMBER 10 CURRENT WINDOWS VERSION IS V8.01c, CURRENT
             MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
             AND CURRENT DISCOVER FILE IS DATED 25 SEPTEMBER 2006.
NEWS HOURS
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             Welcome Banner and News Items
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FILE 'HOME' ENTERED AT 14:02:11 ON 21 JUN 2007

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FULL ESTIMATED COST

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STRUCTURE FILE UPDATES: 20 JUN 2007 HIGHEST RN 938114-25-1 DICTIONARY FILE UPDATES: 20 JUN 2007 HIGHEST RN 938114-25-1

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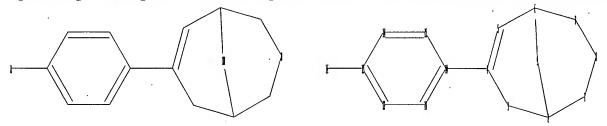
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chain nodes :

16

ring nodes :

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15

chain bonds : 4-10 13-16 ring bonds :

1-2 1-8 2-3 2-9 3-4 4-5 5-6 6-7 6-9 7-8 10-11 10-15 11-12 12-13 13-14

14-15

exact/norm bonds :

1-2 1-8 2-3 2-9 3-4 4-5 5-6 6-7 6-9 7-8 13-16

exact bonds :

4-10

normalized bonds :

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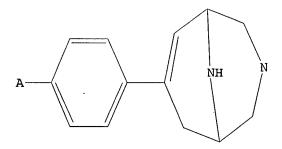
Match level :

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L1 STRUCTURE UPLOADED

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L1 HAS NO ANSWERS



Structure attributes must be viewed using STN Express query preparation.

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SAMPLE SEARCH INITIATED 14:03:17 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 2125 TO ITERATE

94.1% PROCESSED

2000 ITERATIONS

50 ANSWERS

INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:

ONLINE **COMPLETE**

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PROJECTED ITERATIONS:

39735 TO 45265

PROJECTED ANSWERS:

1182 TO

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50 SEA SSS SAM L1

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FULL SEARCH INITIATED 14:03:22 FILE 'REGISTRY'

FULL SCREEN SEARCH COMPLETED -

42642 TO ITERATE

100.0% PROCESSED

42642 ITERATIONS

1597 ANSWERS

SEARCH TIME: 00.00.01

L3 1597 SEA SSS FUL L1

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COST IN U.S. DOLLARS

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FULL ESTIMATED COST

ENTRY SESSION 172.55 172.76

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L4 ANSWER 1 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:768921 CAPLUS
DOCUMENT NUMBER: 145:188915
TITLE: 7-{4-{2-(2,6-dichloro-4-methylphenoxy)ethoxylphenyl}-3,9-diazabicyclo[3,3.1]non-6-ene-6-carboxylic acid cyclopropyl-(2,3-dimethylbenzyl)amide as inhibitors of

INVENTOR (S):

renin for the treatment of hypertension Bezencon, Olivier: Bur, Daniel: Fischli, Walter: Remen, Lubos: Richard-Bildstein, Sylvie: Sifferlen, Thierry: Weller, Thomas Actelion Pharmaceuticals Ltd., Switz. PCT Int. Appl., 26pp. CODEN: PIXXD2 Patent

PATENT ASSIGNEE(S): SOURCE:

Patent English

DOCUMENT TYPE: LANGUAGE: FAMILY ACC. NUM. COUNT: PATENT INFORMATION:

| ENT | NO. | | | KIN | D | DATE | | | | | | | | D | ATE | |
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REFERENCE COUNT:

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ANSWER 1 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN

(Continued)

AB The invention relates to a novel 3,9-diarabicyclo[3.3.1]nonene derivative I, and the enantiomers thereof, and the use thereof as active ingredients in the preparation of pharmaceutical compns. A multistep preparation of I is described as well as resolution of the racemate to provide II. In renin inhibition assays, II displayed ICSO value of 0.3 nM. The invention also concerns related aspects including pharmaceutical compns. containing at least one compound of formula I or II and especially their use as inhibitors of renin.

compound of formula I or II and especially their use as annual renin.

17 903579-35-1P
RL: PAC (Pharmacological activity); PEP (Physical, engineering or chemical
process); PYP (Physical process); SPN (Synthetic preparation); THU
(Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC
(Process); USES (Uses)
(preparation of
[[(dichloromethylphenoxy)ethoxy]phenyl]diazabicyclo[3.3.1]no
nenecarboxylic acid cyclopropyl(dimethylbenzyl)amide as inhibitors of
renin for the treatment of hypertension)
RN 903579-35-1 CAPLUS
CN 3,-9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide,
N-cyclopropyl-7-[4-[2-(2,6dichloro-4-methylphenoxy)ethoxy]phenyl]-N-[(2,3-dimethylphenyl)methyl](9CI) (CA INDEX NAME)

L4 ANSWER 2 OF 15 CAPLUS COPYRIGHT 2007 ACS ON STN
ACCESSION NUMBER: 2006:606520 CAPLUS
DOCUMENT NUMBER: 145:25930
TITLE: Heteroaryl-substituted azabicyclonomene derivatives

INVENTOR (S):

renin inhibitors, their preparation, pharmaceutical compositions, and use in therapy Bezencen, olivier; Boss, Christoph; Bur, Daniel; Corminboeuf, Olivier; Flachil, Walter; Grisostomi, Corinna; Remen, Lubos; Richard-Bildstein, Sylvia; Sifferlen, Thierry; Weller, Thomas Actelion Pharmaceuticals Ltd., Switz. PCT Int. Appl., 70 pp. CODEN: PIXXD2 Patent English

PATENT ASSIGNEE(S): SOURCE:

DOCUMENT TYPE: LANGUAGE: FAMILY ACC. NUM. COUNT: PATENT INFORMATION

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OTHER SOURCE(S):

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* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

MARPAT 145:62930

The invention relates to heteroaryl-substituted azabicyclononene derivs. I, which are renin inhibitors. In compds. I, X is (un)substituted N, O, or S: V is -1.1-2.1-2, where L is -0.012- or -0.012- l is a bond, O, or CH2, and Z is 5-membered heteroarylene containing 2 or 3 heteroatoms

ANSWER 2 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN (Continued) independently selected from N, O, and S; U is (unjsubstituted phenyl; R1 is C1-7 alkyl or C3-6 cycloalkyl; and R2 is (unjsubstituted phenyl; including stereoisomers, racemates, salts, solvates and morphol. forms thereof. The invention also relates to the prepn. of I, pharmaceutical compns. contg. a compd. according to formula I and a pharmaceutically acceptable carrier material, as well as to the use of the compns. for the treatment of cardiovascular events and renal insufficiency. Metal-halogen

exchange of (4-bromophenoxy)triisopropylsilane followed by substitution

triflate II, demethylation, N-Boc-protection, and ester hydrolysis gave the carboxylic acid, which was amidated with N-cyclopropyl-2,3-dichlorobenzylamine and desilylated to give phenol III. Condensation of 2-chloro-3,6-difluorobenzaldehyde with hydroxylamine followed by heterocyclization with 3-(tert-butyldimethylsilyloxy)propyne and desilylation gave [3-(2-chloro-3,6-difluorophenyl)isoxzol-5-yl]methanol, which underwent coupling with phenol III and deprotection, resulting in the formation of IV. Compd. IV expresses an IC50 value of 0.8 nM in an assay for inhibition of human recombinant renin.
890934-57-3P, (1R,5S)-7-[4-[{3-(2-Chloro-3,6-

Absolute stereochemistry.

890846-78-3P, 7-[4-[[5-{2-Chloro-3,6-difluorophenyl][1,2,4]oxadiazol-3-yl}methoxy]phenyl}-3,9-diazabicyclo[3.3.1}non-6-ene-6carboxamide N-cycloproyl-N-{3-methoxy-2-methylbenzyl}
890846-79-4P, 7-[4-[[5-{2-Chlorophenyl}-1],2,4]oxadiazol-3yl]methoxy]phenyl]-3,9-diazabicyclo[3.3.1]non-6-ene-6-carboxamide
N-cycloproyl-N-{3-methoxy-2-methylbenzyl} 890846-80-7P,
7-[4-[2-[3-[2,3-Dichlorophenyl]-[1,2,4]oxadiazol-5-yl]ethyl]phenyl]-3,9diazabicyclo[3.3.1]non-6-ene-6-carboxamide N-cyclopropyl-N-[3-methoxy-2methylbenzyl] 890846-81-8P, 7-[4-[2-[3-(2,6-Dichlorophenyl)-IT

ANSWER 2 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN (Continued 890934-74-4P, 7-[4-[[3-(3-Chloro-6-fluoro-2-trifluoromethylphenyl]isoxazol-5-yl]methoxylphenyl]-3,9-diazabicyclo[3,3.1]mon-6-ene-6-carboxamide N-cyclopropyl-N-(2,3-dichlorobenzyl) 890934-75-5P, 7-[4-[[3-(2,6-

Dimethylphenyl)isoxazol-5-yl]methoxylphenyl]-3,9-diazabicyclo{3.3.1}non-6-ene-6-carboxamide N-cyclopropyl-N-(2,3-dichlorobenzyl)
890934-76-6P, 7-(4-[3-(2,5-bichlorobenyl)isoxazol-5yl]methoxylphenyl]-3,9-diazabicyclo[3,3.1]non-6-ene-6-carboxamide
N-cyclopropyl-N-(2,3-dichlorobenzyl)
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
(Uses)
(drug candidate; prepn. of azabicyclononene derivs. as renin
inhibitors)
RN 890846-78-3 CAPLUS
CN 3,9-biazabicyclo[3,3.1]non-6-ene-6-carboxamide, 7-{4-[5-(2-chloro-3,6difluorophenyl]-1,2,4-oxadiazol-3-yl]methoxylphenyl]-N-cyclopropyl-N-[(3methoxy-2-methylphenyl)methyl)- (9CI) (CA INDEX NAME)

890846-79-4 CAPLUS
3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide,
-[[5-[2-chlorophenyl]1,2,4-oxadiazol-3-yl]methoxy]phenyl]-N-cyclopropyl-N-[(3-methoxy-2-methylphenyl)methyl]- (9CI) (CA INDEX NAME)

890846-80-7 CAPLUS
3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide, N-cyclopropyl-7-[4-[2-[3-[2,3-dichlorophenyl]-1,2,4-oxadiazol-5-yl]ethyl]phenyl]-N-[(3-methoxy-2-methylphenyl)methyl]- (9CI) (CA INDEX NAME)

ANSWER 2 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
[1,2,4]oxadiazol-5-yl]ethyl]phenyl]-3,9-diazabicyclo[3.3.1]non-6-ene-6-carboxamide N-cyclopropyl-N-(3-methoxy-2-methylbenzyl)
890846-92-9p, 7-[4-[[3-(2-chloro-3,6-difluorophenyl)[1,2,4]oxadiazol-5-yl]methoxy]phenyl]-3,9-diazabicyclo[3.3.1]non-6-ene-6-carboxamide N-cyclopropyl-N-(2,3-dichlorobenzyl) 990934-54-0P,
7-[4-[[2-(2-chloro-3,6-difluorophenyl)oxazol-4-yl]methoxy]phenyl]-3,9-diazabicyclo[3.3.1]non-6-ene-6-carboxamide N-cyclopropyl-N-(2,3-dichlorobenzyl) 890934-55-1P, 7-[4-[[5-(2-chloro-3,6-dichlorobenzyl)] 890934-55-1P, 7-[4-[[5-(2-chloro-3,6-dichlorobenzyl)]]

difluorophenyl)isoxazol-3-yl}methoxy]phenyl)-3,9-diazabicyclo[3.3.1]non-6-ene-6-carboxamide N-cyclopropyl-N-{2,3-dichlorobenzyl] 890934-56-2P, (1R,55)-3-Acetyl-7-[4-[[3-{2-chloro-3,6-

difluorophenyl)isoxazol-5-yl]methoxy]phenyl]-3,9-diazabicyclo[3.3.1]non-6ene-6-carboxamide N-cyclopropyl-N-{2,3-dichlorobenzyl]
890934-58-4P, 7-[4-[13-[4-Fluoro-2-trifluoromethylphenyl)isoxazol5-yl]methoxy]phenyl]-3,9-diazabicyclo[3.3.1]non-6-ene-6-carboxamide
N-cyclopropyl-N-{2,3-dichlorobenzyl] 990934-59-5P,
7-[4-[3-(2-chloro-6-fluorophenyl)isoxazol-5-yl]methoxy]phenyl]-3,9diazabicyclo[3.3.1]non-6-ene-6-carboxamide N-cyclopropyl-N-{2,3dichlorobenzyl] 890934-60-8P, 7-[4-[[3-(2,5-

Difluorophenyl)isoxazol-5-yllmethoxylphenyl]-3,9-diazabicyclo[3.3.1]non-6-ene-6-carboxamide N-cyclopropyl-N-{2,3-dichlorobenzyl)
890934-61-9F, 7-{4-{13-{2-Chioro-4-fluorophenyl]isoxazol-5yl]methoxylphenyl]-3,9-diazabicyclo[3.3.1]non-6-ene-6-carboxamide
N-cyclopropyl-N-{2,3-dichlorobenzyl] 890934-62-0F,
7-{4-{13-{5-Chioro-1,3-dimethyl-1H-pyrazol-4-yl]isoxazol-5yl]methoxylphenyl]-3,9-diazabicyclo[3.3.1]non-6-ene-6-carboxamide
N-cyclopropyl-N-{2,3-dichlorobenzyl] 890934-63-1F,
7-{4-{13-{2,4-Dichlorophenyl]isoxazol-5-yl]methoxylphenyl]-3,9diazabicyclo[3.3.1]non-6-ene-6-carboxamide N-cyclopropyl-N-{2,3-dichlorobenzyl] 890934-64-2F, 7-[4-{13-{2,6-}}}

Dichlorophenyl)isoxazol-5-yl]methoxy]phenyl]-3,9-diazabicyclo[3.3.1]non-6-ene-6-carboxamide N-cyclopropyl-N-[2,3-dichlorobenzyl]
890934-65-3P, 7-[4-[3-[2,3,6-Trichlorophenyl]isoxazol-5-yl]methoxy]phenyl]-3,9-diazabicyclo[3.3.1]non-6-ene-6-carboxamide
N-cyclopropyl-N-[2,3-dichlorobenzyl] 890934-66-4P,
7-[4-[3-(2-Fluoro-6-trifluoromethylphenyl]isoxazol-5-yl]methoxy]phenyl]-3,9-diazabicyclo[3.3.1]non-6-ene-6-carboxamide N-cyclopropyl-N-[2,3-dichlorobenzyl] 890934-67-5P, 7-[4-[[3-[2,3-

difluorophenyl)isoxazol-5-yl]methoxy]phenyl]-3,9-diazabicyclo[3.3.1]non-6-ene-6-carboxamide N-cyclopropyl-N-(2,3-dichlorobenzyl)

ANSWER 2 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN

890846-81-8 CAPLUS
3,9-Diazabicyclo[3,3,1]non-6-ene-6-carboxamide, N-cyclopropyl-7-[4-{2-[3-(2,6-dichlorophenyl]-1,2,4-oxadiazol-5-yl]ethyl]phenyl]-N-[(3-methoxy-2-methylphenyl)methyl]- (9CI) (CA INDEX NAME)

890846-82-9 CAPLUS 3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide, 7-{4-[[3-{2-chloro-3,6-

difluoropheny1)-1,2,4-oxadiazol-5-yl]methoxy]phenyl]-N-cyclopropyl-N-[(2,3-dichlorophenyl)methyl]- (9CI) (CA INDEX NAME)

890934-54-0 CAPLUS
3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide, 7-[4-[[2-(2-chloro-3,6-difluorophenyl)-4-oxazolyl]methoxy[phenyl]-N-cyclopropyl-N-[(2,3-dichlorophenyl)methyl]- (9CI) (CA INDEX NAME)

RN 890934-55-1 CAPLUS
3,9-Diazabicyclo[3.3.]]non-6-ene-6-carboxamide, 7-[4-[(5-(2-chloro-3,6-difluorophenyl)-3-isoxazolyl]methoxylphenyl]-N-cyclopropyl-N-[(2,3-dichlorophenyl)methyl]- (9CI) (CA INDEX NAME)

(Continued)

RN 890934-56-2 CAPLUS
CN 3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide, 3-acetyl-7-[4-[[3-(2-chloro-3,6-difluorophenyl]-5-isoxazolyl]methoxy[phenyl]-N-cyclopropyl-N-[(2,3-dichlorophenyl)methyl]-, (1R,58)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 2 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 890934-61-9 CAPLUS
3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide, 7-[4-[[3-{2-chloro-4-fluorophenyl}-5-isoxazolyl]methoxy]phenyl}-N-cyclopropyl-N-[{2,3-dichlorophenyl}methyl]- (9CI) (CA INDEX NAME)

RN 890934-62-0 CAPLUS
3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide, 7-[4-[[3-[5-chloro-1,3-dimethyl-1H-pytrazol-4-yl]-5-isoxazolyl]methoxylphenyl]-N-cyclopropyl-N-[(2,3-dichlorophenyl)methyl]- (9CI) (CA INDEX NAME)

RN 890934-63-1 CAPLUS
CN 3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide, N-cyclopropyl-7-[4-{[3-(2,4-dichlorophenyl]-5-isoxazolyl]methoxylphenyl]-N-[{2,3-dichlorophenyl]methyl}- (9CI) (CA INDEX NAME)

AC N NH NH O NH C1

RN 890934-58-4 CAPLUS
CN 3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide, N-cyclopropyl-N-[(2,3-dichlorophenyl)methyl)-7-[4-{[3-[4-fluoro-2-(trifluoromethyl)phenyl]-5-isoxazolyl]methoxy]phenyl]- 9CI) (CA INDEX NAME)

RN 890934-59-5 CAPLUS
3,9-Dlazablcyclo[3.3.1]non-6-ene-6-carboxamide, 7-[4-{[3-{2-chloro-6-fluorophenyl}-5-isoxazolyl]methoxy]phenyl]-N-cyclopropyl-N-{{2,3-dichlorophenyl}methyl}- (9CI) (CA INDEX NAME)

RN 890934-60-8 CAPLUS
CN 3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide, N-cyclopropyl-N-[(2,3-dichlorophenyl)methyl]-7-[4-[[3-(2,5-difluorophenyl)-5-isoxazolyl]methoxy]phenyl)- (SCI) (CA INDEX NAME)

L4 ANSWER 2 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 890934-64-2 CAPLUS
CN 3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide, N-cyclopropyl-7-[4-[[3-(2,6-dichlorophenyl)-5-isoxazolyl]methoxy]phenyl]-N-[(2,3-dichlorophenyl)methyl]- (9CI) (CA INDEX NAME)

RN 890934-65-3 CAPLUS
CN 3,9-Dlazabicyclo[3.3.1]non-6-ene-6-carboxamide, N-cyclopropyl-N-[(2,3-dichlorophenyl)methyl)-7-(4-[(3-(2,3,6-trichlorophenyl)-5-isoxazolyl]methoxy]phenyl]- (9CI) (CA INDEX NAME)

RN 890934-66-4 CAPLUS

ON 3,9-Dlazabicyclo[3.3.1]non-6-ene-6-carboxamide, N-cyclopropyl-N-[{2,3-dichlorophenyl|methyl]-7-[4-{[3-[2-fluoro-6-(trifluoromethyl)phenyl]-5-isoxazolyl]methoxy]phenyl]- (9CI) (CA INDEX NAME)

890934-67-5 CAPLUS
3,9-Diazabicyclo(3.3.1]non-6-ene-6-carboxamide, N-cyclopropyl-7-{4-{{3-(2,3-dichlorophenyl)-5-isoxazolyl]methoxy]phenyl}-N-{{2,3-dichlorophenyl)methyl}- (9CI) (CA INDEX NAME)

890934-68-6 CAPLUS 3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide, 7-[4-[[3-{2-chloro-6-

fluoro-3-methylphenyl)-5-isoxazolyl]methoxy]phenyl]-N-cyclopropyl-N-[(2,3-dichlorophenyl)methyl]- (9CI) (CA INDEX NAME)

890934-69-7 CAPLUS 3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamidé, 7-[4-[[3-(3-chloro-2-fluorophenyl]-5-isoxazolyl]methoxylphenyl]-N-cyclopropyl-N-[(2,3-dichlorophenyl)methyl]- (9CI) (CA INDEX NAME)

ANSWER 2 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN

890934-74-4 CAPLUS
3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide, 7-[4-[[3-[3-chloro-6-fluoro-2-(trifluoromethyl)phenyl]-5-iaoxazolyl]methoxylphenyl]-N-cyclopropyl-N-[(2,3-dichlorophenyl)methyl]- (9CI) (CA INDEX NAME)

890934-75-5 CAPLUS
3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide, N-cyclopropyl-N-{(2,3-dichlorophenyl)methyl]-7-[4-{[3-(2,6-dlmethylphenyl)-5- isoxazolyl]methoxy)phenyl}- (9CI) (CA INDEX NAME)

890934-76-6 CAPLUS
3,9-Dlazabicyclo[3.3.1]non-6-ene-6-carboxamide, N-cyclopropyl-7-[4-[[3-(2.5-dichlorophenyl)-5-isoxazolyl]methoxy[phenyl]-N-[(2,3-dichlorophenyl)methyl]- (9CI) (CA INDEX NAME)

890934-70-0 CAPLUS 3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide, 7-[4-[[3-(6-chloro-2-

fluoro-3-methylphenyl)-5-isoxazolyl]methoxy]phenyl]-N-cyclopropyl-N-{(2,3-dichlorophenyl)methyl}- (9CI) (CA INDEX NAME)

890934-71-1 CAPLUS
3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide, 7-[4-[[3-[3-chloro-2-fluoro-6-(ctrifluoromethyl)phenyl]-5-isoxazolyl]methoxy]phenyl]-N-cyclopropyl-N-[[2,3-dichlorophenyl]methyl]- (9CI) (CA INDEX NAME)

890934-73-3. CAPLUS
3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide, 7-{4-[3-{3-chloro-2,6-difluorophenyl}-5-isoxazolyl]methoxy]phenyl]-N-cyclopropyl-N-[(2,3-dichlorophenyl)methyl]- (9CI) (CA INDEX NAME)

ANSWER 2 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN

890846-83-0P, 7-{4-{3-{2-chloro-3,6-difluorophenyl}}isoxazol-5-yllmethoxy|phenyl]-3,9-diazabicyclo[3.3.1}non-6-ene-6-carboxamide N-cyclopropyl-N-(2,3-dichlorobenzyl) RL: PAC (Pharmacological activity); PEP (Physical, engineering or

cai process); PYP (Physical process); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses) (Isacemic drug candidate; preparation of azabicyclononene derivs. as

renin

n inhibitors)
890846-83-0 CAPLUS
3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide, 7-[4-[[3-{2-chloro-3,6-difluorophenyl]-5-isoxazolyl]methoxy]phenyl]-N-cyclopropyl-N-[(2,3-dichlorophenyl)methyl]- (9CI) (CA INDEX NAME)

REFERENCE COUNT:

THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

ANSWER 3 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN ACCESSION NUMBER

2006:606519 CAPLUS 145:83392

DOCUMENT NUMBER: TITLE:

Heteroaryl-substituted diazabicyclononene derivatives as renin inhibitors, their preparation,

pharmaceutical

compositions, and use in therapy
Bezencon, Olivier; Remen, Lubos; Sifferlen, Thierry;
Grisostomi, Corinna; Richard-Bildstein, Sylvia; Bur,
Daniel: Boss, Christoph; Corminboeuf, Olivier;
Fischli, Walter; Weller, Thomas
Actelion Phermaceuticals Ltd., Switz.
PCT Int. Appl., 40 pp.
CODEN: PIXXD2
Patent
English
2 INVENTOR (S):

PATENT ASSIGNEE(S): SOURCE:

DOCUMENT TYPE:

FAMILY ACC. NUM. COUNT:

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OTHER SOURCE(S):

MARPAT 145:83392

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

The invention relates to heteroaryl-substituted diazabicyclononene

s.

I, which are renin inhibitors. In compds. I, V is -L1-2-L2-, where L1 is -OCH2- or -CH2CH2-, L2 is a bond, -O-, or -CH2-, and Z is 5-membered

ANSWER 3 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN

890846-79-4 CAPLUS
3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide,
-[[5-(2-chlorophenyl]1,2,4-oxadiazol-3-yl]methoxy]phenyl]-N-cyclopropyl-N-[(3-methoxy-2-methylphenyl)methyl]- (9CI) (CA INDEX NAME)

890846-80-7 CAPLUS
3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide, N-cyclopropyl-7-[4-[2-[3-(2,3-dichlorophenyl)-1,2,4-oxadiazol-5-yl]ethyl]phenyl]-N-[(3-methoxy-2-methylphenyl)methyl]- (9CI) (CA INDEX NAME)

890846-81-8 CAPLUS
3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide, N-cyclopropyl-7-[4-[2-[3-(2,6-dichlorophenyl)-1,2,4-oxadiazol-5-yl]ethyl]phenyl]-N-[[3-methoxy-2-methylphenyl]methyl]- (9CI) (CA INDEX NAME)

890846-82-9 CAPLUS 3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide, 7-[4-[[3-(2-chloro-3,6-

difluorophenyl)-1,2,4-oxadiazol-5-yl]methoxy]phenyl]-N-cyclopropyl-N-[(2,3-

ANSWER 3 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN (Continued) heteroarylene contg. 2 or 3 heteroatoms; U is (un)substituted phenyl; Rl is Cl-7 alkyl or C3-6 cycloalkyl; and R2 is (un)substituted phenyl; Rl including stereoisomers, racemates, salts, solvates and morphol. forms thereof. The invention also relates to the prepn. of I, pharmaceutical compns. contg. at least one compd. according to formula I and pharmaceutically acceptable carrier materials or adjuvants, as well as to the use of the compns. for the treatment of cardiovascular events and renal insufficiency. Metal-halogen exchange of (4-bromophenoxyltriisopropylsilane followed by substitution of triflate II, demethylation, N-Boc-protection, and ester hydrolysis gave the carboxylic acid, which was amidated with N-cyclopropyl-2,3-dichlorobenylamine and desilylated to give phenol III. Condensacion of 2-chloro-3,6-difluorobenzaldehyde with hydroxylamine followed by heterocyclization

3-(tert-butyldimethylsilyloxy)propyne and desilylation gave [3-(2-chloro-3,6-difluorophenyl)isoxazol-5-yl]methanol, which underwent coupling with phenol III and ester cleavage, resulting in the formation

Compd. IV expresses an IC50 value of 0.8 nM in an assay for

IV. Compd. IV expresses an IC50 value of 0.8 nM in an assay for inhibition of human recombinant renin. 890846-78-3P, 7-{4-[15-(2-Chloro-3,6-diflucrophenyl)-(1.2,4]oxadiazol-3-yl]methoxy|phenyl]-3,9-diazabicyclo(3.3.1]non-6-ene-6-carboxamide N-cyclopropyl-N-(3-methoxy-2-methylbenzyl) 890846-79-4P, 7-[4-[5-(2-Chlorophenyl]-[1,2,4]oxadiazol-3-yl]methoxy|phenyl]-3,9-diazabicyclo(3.3.1]non-6-ene-6-carboxamide N-cyclopropyl-N-(3-methoxy-2-methylbenzyl) 890846-80-7P, 7-(4-[2-[3-(2,3-bichlorophenyl]-[1,2,4]oxadiazol-5-yl]ethyl]phenyl]-3,9-diazabicyclo(3.3.1]non-6-ene-6-carboxamide N-cyclopropyl-N-(3-methoxy-2-methylbenzyl) 890846-81-8P, 7-[4-[2-[3-(2,6-Dichlorophenyl]-(1,2,4]oxadiazol-5-yl]ethyl]phenyl]-3,9-diazabicyclo[3.3.1]non-6-ene-6-carboxamide N-cyclopropyl-N-(3-methoxy-2-methylbenzyl) 890846-83-0P, 7-[4-[[3-(2-Chloro-3,6-diflucrophenyl)]-3,9-diazabicyclo[3.3.1]non-6-ene-6-carboxamide N-cyclopropyl-N-(2,3-dichlorobenzyl) 890846-83-0P, 7-[4-[[3-(2-Chloro-3,6-diflucrophenyl)] 890846-83-0P, 7-[4-[3-(2-Chloro-3,6-diflucrophenyl)] 890846-83-0P, 80098-800 IT

ANSWER 3 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN dichlorophenyl)methyl]- (9CI) {CA INDEX NAME}

890846-83-0 CAPLUS
3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide, 7-[4-[3-[2-chloro-3,6-difluorophenyl]-5-isoxazolyl]methoxy]phenyl]-N-cyclopropyl-N-[(2,3-dichlorophenyl)methyl]- (9CI) (CA INDEX NAME)

REFERENCE COUNT:

THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L4 ANSWER 4 OF 15
ACCESSION NUMBER:
DOCUMENT NUMBER:
15:46095
Dlazabloyclononene derivatives as renin inhibitors, their preparation, pharmaceutical compositions, and use in therapy
Bezencon, Olivier: Bur, Daniel; Fischli, Walter; Remen, Lubos; Richard-Bildstein, Sylvia: Sifferien, Thierry; Weber, Hans-Peter: Weller, Thomas
Actelion Pharmaceuticals Ltd., Switz.
PATENT ASSIGNEE(S):
SOURCE:
DOCUMENT TYPE:
DOCUMENT TYPE:
DAMGUAGE:

English

English LANGUAGE:

FAMILY ACC. NUM. COUNT: PATENT INFORMATION:

GI

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| | ₩O | 2006 | 0617 | 91 | | A2 | | 2006 | 0615 | | WO 2 | 005- | IB54 | 113 | | 2 | 0051 | 208 | |
| | WO | 2006 | 0617 | 91 | | A3 | | 2006 | 0810 | | | | | | | | | | |
| | | W: | ΑE, | AG, | AL, | AM, | AT, | ΑU, | AZ, | BA, | BB, | BG, | BR, | BW, | BY, | BZ, | CA, | CH, | |
| | | | CN, | co, | CR. | CU, | CŻ, | DE, | DK, | DM. | DZ, | EC. | EE, | EG, | ES, | FI, | GB, | GD, | |
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| | | | KZ, | LC, | LK, | LR, | LS, | LT, | LU, | LV, | LY, | MA, | MD, | MG, | MK, | MN, | MW. | MX, | |
| | | | MZ, | NA, | NG, | NI, | NO, | NZ, | OM, | PG, | PH, | PL, | PT, | RO, | RU, | SC, | SD, | SE, | |
| | | | SG, | SK, | SL, | SM, | SY, | TJ, | TM. | TN, | TR, | TT, | TZ, | UA, | UG, | US, | υz, | VC, | |
| | | | VN, | YU, | ZA, | ZM, | ZW | | | | | | | | | | | | |
| | | RW: | AT, | BE, | BG, | CH, | CY, | CZ, | DE, | DK, | EE, | ES, | FI, | FR, | GB, | GR, | HU, | IE, | |
| | | | IS, | IT, | LT, | LU, | LV, | MC, | NL, | PL, | PT, | RO, | SE, | SI, | SK, | TR, | BF, | ВJ, | |
| | | | CF, | CG, | CI, | CM, | GΑ, | GN, | GQ, | GW, | ML, | MR, | ΝE, | SN, | TD, | TG, | BW, | GH, | |
| | | | GM, | KE, | LS, | MW, | MZ, | NA, | SD, | SL, | sz, | TZ, | UG, | ZM, | ZW, | AM, | ΑZ, | BY, | |
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| PRIO | RIT | (APP | LN. | INFO | .: | | | | | | WO 2 | 004- | EP13 | 949 | | A 2 | 0041 | 208 | |
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* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to diazabicyclononene derivative I, the racemate as well as the individual enantiomers thereof, which are renin inhibitors. The invention also relates to the preparation of I, pharmaceutical compns. containing compound I and a pharmaceutically acceptable carrier material, as well

as to
the use of the compns. for the treatment of cardiovascular events and
renal insufficiency. Preparation of Grignard reagent from
1,4-dibromobenzene
followed by substitution of allyl bromide, hydroboration, oxidation, and
protection with tert-butyldimethylsilyl chloride gave bromide II.
O-Trifluoromethanesulfonylation of III followed by substitution with
lithiated II, demethylation, desilylation, N-protection, and coupling with

2-chloro-3,6-difluorophenol gave ether IV, which underwent ester hydrolysis, amidation with N-cyclopropyl-2,3-dichlorobenzylamine, deprotection, and chiral HPLC to give (1R,5S)-diazabicyclononene I. Compound (1R,5S)-I expresses an IC50 value of 0.5 mk in an assay for

ANSWER 4 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN

ANSWER 4 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN inhibition of human recombinant renin. 889881-63-4P (Continued)

889881-63-49"
RI: PAC (Pharmacological activity); PUR (Purification or recovery); THU
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
(USes)
(chiral drug candidate; preparation of diazabicyclononene derivs. as

n
inhibitors)
889881-63-4 CAPLUS
3,9-Dlazabicyclo[3.3.1]non-6-ene-6-carboxamide, 7-{4-[3-(2-chloro-3,6-difluorophenoxy)propyl]phenyl]-N-cyclopropyl-N-{(2,3-dichlorophenyl)methyl]-, (1R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

889881-62-3P
RL: PAC (Pharmacological activity); PEP (Physical, engineering or nical process); PYP (Physical process); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses) (racemic drug candidate; preparation of diazabicyclononene derivs. as

n inhibitors)
889881-62-3 CAPLUS
3,9-Dlazabicyclo{3.3.1]non-6-ene-6-carboxamide, 7-[4-[3-(2-chloro-3,6-difluorophenoxy)propyl]phenyl]-N-cyclopropyl-N-[{2,3-dichlorophenyl)methyl]- (9CI) (CA INDEX NAME)

L4 ANSWER 5 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:542922 CAPLUS
DOCUMENT NUMBER: 145:28021
TITLE: Bicyclic lactam derivatives as renin inhibitors,
their

INVENTOR (S):

preparation, pharmaceutical compositions, and use in therapy

preparation, pharmaceutical compositions, and use therapy
Bezencon, Olivier; Boss, Christoph; Bur, Daniel;
Corminboeuf, Olivier; Fischli, Walter; Grisostomi,
Corinna; Remen, Lubos; Richard-Bildstein, Sylvia;
Sifferlen, Thierry; Weller, Thomas
Actelion Pharmaceuticals Ltd., Switz.
PCT Int. Appl., 24 pp.
CODEN: PIXXD2
Patent

PATENT ASSIGNEE(S): SOURCE:

OTHER SOURCE(S):

Patent English 2

LANGUAGE: FAMILY ACC. NUM. COUNT: PATENT INFORMATION:

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| | 2006 | | | | A2 | | 2006 | | | WO 2 | 005- | IB54 | 800 | | 2 | 0051 | 201 |
| WO | 2006 | 0593 | 04 | | A3 | | 2006 | 1012 | | | | | | | | | |
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| | | ΚZ, | LC, | LK, | LR, | LS, | LT, | LU, | LV, | LY, | MA, | MD, | MG, | MK, | MN, | MW, | MX, |
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| WO | 2006 | | | | | | | | | | | | | | | | |
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| | | | | | TJ, | TM | | | | | | | | | | | |
| PRIORIT | Y APP | LN. | INFO | .: | | | | | , | WO 2 | 004- | EP13 | 610 | | A 2 | 0041 | 201 |

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

MARPAT 145:28021

The invention relates to bicyclic lactam derivs. of formula I, which are renin inhibitors. In compds. I, W is 1,4-disubstituted phenylene: V is oxyalkyl, alkoxy, or oxyalkoy, V is (un)substituted phenyl: T is -C(0)N(R1)-, where R1 is alkyl or cycloalkyl; Q is alkylene; M is

ANSWER 5 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
(un)substituted Ph or (un)substituted pyridinyl; and J is H or lower
alkyl; including stereoisomers, solvates, polymorphs, and salts thereof.
The invention also relates to the prepn. of I, pharmaceutical compns.
contg. at least one compd. I and a pharmaceutically acceptable carrier
material, as well as to the use of the compns. for the treatment of
cardiovascular events and renal insufficiency. N-Protection of
DL-allylglycine followed by amidation with N-methylglycinate, cyclizative
deprotection, carboxylation, and hydride redn. gave piperazinone II,
th

which
was cyclized, oxidized, and carboxylated, resulting in the formation of
bicyclic compd. III. O-Trifluoromethanesulfonylation of III followed by
substitution with lithiated
4-(3-(tert-butyldimethylsityloxy)propyl]phenyl
bromide, desilylation, and coupling with 2-chloro-3,6-difluorophenol gave
ether IV, which underwent ester cleavage, amidation with
N-cyclopropyl-2,3-dichlorobenzylamine, and carbamate removal to give
bicyclic lactam V. Compd. V expresses IC50 value below 10 nM in an assay
for inhibition of human recombinant renth.
IT 889128-15-8P
RL: PRC (Pharmacological activity); SPN (Synthetic preparation); THU
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
(Uses)

(drug candidate; preparation of bicyclic lactam derivs. as renin

ANSWER 6 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN (Continued) alkylene; M is (un)substituted phenyl; and J is H or lower alkyl; including stereoisomers, solvates, polymorphs, and salts thereof. The invention also relates to the prepn. of I, pharmaceutical compns. contg. at least one compd. I and pharmaceutically acceptable carrier materials

adjuvants, as well as to the use of the compns. for the treatment of cardiovascular events and renal insufficiency. N-Protection of Di-allylglycine followed by amidation with N-methylglycinate, cyclizative deprotection, carboxylation, and hydride redn. gave piperazinone II,

h was cyclized, oxidized, and carboxylated, resulting in the formation of bicyclic compd. III. O-Trifluoromethanesulfonylation of III followed by substitution with lithiated - (tert-butyldimethylsilyloxy)propyl]phenyl bromide, desilylation, and coupling with 2-chloro-3,6-difluorophenol gave ether IV, which underwent ester cleavage, amidation with N-cyclopropyl-2,3-dichlorobenylamine, and carbamate removal to give bicyclic lactam V. Compd. V expresses ICSO value of 2.1 nM in an assay for inhibition of human recombinant remin. 889128-15-8P

889128-15-8P RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES

(drug candidate; preparation of bicyclic lactam derivs. as renin

(drug candidate; inhibitors) RN 889128-15-8 CAPLUS CN 3,9-Diazabicvclof3

3/9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide, 7-[4-[3-(2-chloro-3,6-difluorophenoxy)propyl)phenyl]-N-cyclopropyl-N-[(2,3-dichlorophenyl)methyl]-3-methyl-2-oxo- (9CI) (CA INDEX NAME)

REFERENCE COUNT:

THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L4 ANSWER 6 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:542920 CAPLUS
DOCUMENT NUMBER: 145:28020
TITLE: Bicyclic lactam derivatives as renin inhibitors,

preparation, pharmaceutical compositions, and use in therapy
Bezencon, Olivier; Remen, Lubos; Sifferlen, Thierry;
Bezencon, Olivier; Remen, Lubos; Sifferlen, Thierry;
Grisostomi, Corinna; Richard-Bildstein, Sylvia; Bur,
Daniel; Boss, Christoph; Corminboeuf, Olivier;
Fischli, Walter; Weller, Thomas
Actelion Pharmaceuticals Ltd., Switz.
PCT Int. Appl., 27 pp.
CODEN: PIXXD2 INVENTOR (S):

PATENT ASSIGNEE(S): SOURCE:

DOCUMENT TYPE: LANGUAGE: Patent English

FAMILY ACC. NUM. COUNT: PATENT INFORMATION:

PATENT NO. APPLICATION NO. KIND DATE DATE

OTHER SOURCE(S): MARPAT 145:28020

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

The invention relates to bicyclic lactam derivs. of formula I, which are renin inhibitors. In compds. I, W is 1,4-disubstituted phenylene; V is oxy-lower alkyl, lower alkoxy, or oxy-lower alkoxy; U is (un)substituted aryl; T is -C(0)N(R1)-, where R1 is lower alkyl or cycloalkyl; Q is lower

L4 ANSWER 7 OF 15 CAPLUS COPYRIGHT 2007 ACS ON STN ACCESSION NUMBER: 2006:333438 CAPLUS DOCUMENT NUMBER: 144:350717

Preparation of bicyclonomene derivatives as

inhibitors INVENTOR(S):

of renin
Bezencon, Olivier; Boss, Christoph; Bur, Daniel;
Corminboeuf, Olivier; Fischli, Walter; Grisostomi,
Corinnar Remen, Lubos; Richard, Sylvia; Sifferlen,
Thierry; Weller, Thomas
Actelion Pharmaceuticals Ltd., Switz.
PCT Int. Appl., 87 pp.
CODEN: PIXXD2
Patent

PATENT ASSIGNEE(S): SOURCE:

DOCUMENT TYPE:

LANGUAGE: FAMILY ACC. NUM. COUNT: PATENT INFORMATION:

KIND ----A2 A3 PATENT NO. DATE APPLICATION NO. WO 2006021399 WO 2006021399 20060302 WO 2005-EP9045 20050822 MO 2006021399 A2 20061026

WE AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, LC, LK, LK, LS, LT, LU, LV, MA, MD, MG, MK, NN, NG, NI, NN, NZ, OM, EG, PH, PL, PT, RO, RU, SC, SL, SM, SY, TJ, TM, TM, TR, TT, TZ, UA, UG, US, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, IS, IT, IT, LU, LV, MG, NL, PL, PT, RO, SE, SI, CF, CG, CI, CM, GA, GN, GQ, GW, NL, MR, NE, SN, GM, KE, LS, MW, MZ, NR, SD, SL, SZ, TZ, UG, ZM, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO:: WO 2004-EP9475 BY, ES, KM, MW, SD, UZ, CA, GB, KR, MZ, SG, VN, FI, KP, MX, SE, VC, GD, KZ, NA, SK, YU, CY, CZ, DE, DK, EE, ES, FI, FR, GB, LV, MC, NL, PL, PT, RO, SE, SI, SK, GA, GN, GQ, GW, ML, MR, NE, SN, TD, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, TJ, TM GR, TR, TG, AM,

MARPAT 144:350717

OTHER SOURCE(S):

AB The invention relates to novel bicyclononene derivs. (I) (wherein X = NH, N(L), CH2, CH(L), O, S; W = Ph substituted by V in para-position; V = CH2N(R)-CH2, CH2N(R)-CH2, CH2CH2N(R), N(R)-CH2CH2N(R)-CH2, CH2CH2N(R)-CH2CH2N, CH2CH2N(R)-CH2CH2N, CH2CH2N(R)-CH2CH2N, CH2CH2N, CH2CH2N

treatments with immunosuppressive agents, and other diseases knorelated to the renin-angiotensin system. Thus, 2-chloro-3,6-diffluorobenzaldehyde underwent reductive amination with 6-{cyclopropyl(3-methoxy-2-methylbenzyl)carbamoyl]-7-[4-(2-

methylaminoethyl}phenyl}-3,9-diazabicyclo{3.3.1}non-6-ene-3,9-dicarboxylic

L4 ANSWER 7 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN (Continued) acid di-tert-Bu ester followed by treatment with 4 M HCl/dioxane in CH2C12

to give 7-[4-[2-[(2-Chloro-3,6-difluorobenzyl)methylamino]ethyl]phenyl]3,9-diazabicyclo[3.3.1]non-6-ene-6-carboxylic acid
cyclopropyl[3-methoxy-2methylbenzyl]amide [II]. II showed IC50 of 2.4 nM against recombinant

N-methylamino]methyl]phenyl]-3,9-diazabicyclo[3.3.1]non-6-ene-6-carboxylic acid N-cyclopropyl-N-(3-methoxy-2-methylbenzyl)amide 881849-26-9P

acid N-cyclopropyl-N-(3-methoxy-2-methylbenzyl) amide 881849-26-99
7-[4-[N-(2-Chloro-6-fluoro-3-methylbenzyl)-N-methylamino]methyl]phenyl]3.9-diazabicyclo[3.3.]non-6-ene-6-carboxylic acid N-cyclopropyl-N-(3-methoxy-2-methylbenzyl) amide 881849-27-0p, 7-[4-[[N-(2-Chloro-3,6-difluorobenzyl)-N-methylamino]methyl]phenyl]-3,9-diazabicyclo[3.3.]]non-6-ene-6-carboxylic acid
N-cyclopropyl-N-(3-methoxy-2-methylamino]methyl]phenyl]-3,9-diazabicyclo[3.3.1]non-6-ene-6-carboxylic acid N-cyclopropyl-N-(3-methylamino]methylamino]methylamino]methylamino]methylamino]methylphenyl]-3,9-diazabicyclo[3.3.1]non-6-ene-6-carboxylic acid N-cyclopropyl-N-(3-methoxy-2-methylbenzyl)amide 881849-29-2P, 7-[4-[[N-(2-Chloro-6-fluorobenzyl)-N-methylamino]methyl]phenyl]-3,9-diazabicyclo[3.3.1]non-6-ene-6-carboxylic acid N-cyclopropyl-N-(3-methoxy-2-methylbenzyl)amide 881849-30-5P***, 7-[4-[[N-(2,-3)-chlorobenzyl)-N-methylamino]methyl]phenyl]-3,9-diazabicyclo[3.3.1]non-6-ene-6-carboxylic acid N-cyclopropyl-N-(3-methoxy-2-methylamino]methyl]phenyl]-3,9-diazabicyclo[3.3.1]non-6-ene-6-carboxylic acid N

ANSWER 7 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
7-[4-[[N-Ethyl-N-[2,3,6-trichlorobenzyl]amino]methyl]phenyl]-3,9diazabicyclo[3,3.1]non-6-ene-6-carboxylic acid N-cyclopropyl-N-[2,3dichlorobenzyl]amide 881849-55-4P, 7-[4-[[N-[2-Cyclophenzyl]-Nethylamino]methyl]phenyl]-3,9-diazabicyclo[3,3.1]non-6-ene-6-carboxylic
acid N-cyclopropyl-N-[2,3-dichlorobenzyl]amide 881849-56-5P,
7-[4-[[N-[2,6-bliluorobenzyl]-N-ethylamino]methyl]phenyl]-3,9diazabicyclo[3,3.1]non-6-ene-6-carboxylic acid N-cyclopropyl-N-[2,3dichlorobenzyl]amide 881849-57-6P, 7-[4-[[N-Ethyl-N-[2,4,6trifluorobenzyl]amide 881849-57-6P, 7-[4-[[N-Ethyl-N-[2,4,6trifluorobenzyl]amide 881849-57-6P, 7-[4-[[N-cthyl-N-[2,3dichlorobenzyl]amide 881849-59-9P,
7-[4-[[N-[2,4-Dichlorobenzyl]-N-ethylamino]methyl]]non-6-ene-6-carboxylic
acid N-cyclopropyl-N-[2,3-dichlorobenzyl]amide 881849-59-9P,
7-[4-[[N-[2,4-Dichlorobenzyl]-N-ethylamino]methyl]phenyl]-3,9diazabicyclo[3,3.1]non-6-ene-6-carboxylic acid N-cyclopropyl-N-[2,3dichlorobenzyl]amide 881849-60-1P, 7-[4-[[N-[2-Chloro-6-

dichlorobenzyl) amide 881849-60-1P, 7-[4-[N-(2-Chloro-6-fluorobenzyl)-N-ethylamino]methyl]phenyl]-3,9-diazabicyclo[3,3,1]non-6-ene-6-carboxylic acid N-cyclopropyl-N-(2,3-dichlorobenzyl)amide 881849-61-2P, 7-[4-[N-Ethyl-N-(2-fluoro-5-methoxybenzyl)amido methyl]phenyl]-3,9-diazabicyclo[3,3,1]non-6-ene-6-carboxylic acid N-cyclopropyl-N-(2,3-dichlorobenzyl)amide 881849-62-3P, 7-[4-[N-Ethyl-N-(2-fluoro-6-trifluoromethylbenzyl]amino]methyl]phenyl]-3,9-diazabicyclo[3,3,1]non-6-ene-6-carboxylic acid N-cyclopropyl-N-(2,3-dichlorobenzyl)amide 881849-63-4P, 7-[4-[N-(2,5-Dichlorobenzyl]-N-ethylamino]methyl]phenyl]-3,9-diazabicyclo[3,3,1]non-6-ene-6-carboxylic acid N-cyclopropyl-N-[2,3-dichlorobenzyl]-N-diazabicyclo[3,3,1]non-6-ene-6-carboxylic acid N-cyclopropyl-N-(3,3-dichlorobenzyl)amide 881849-64-5P, 7-[4-[N-(2,6-Dimethylbenzyl)]-N-methylamino]methylphenyl]-3,9-diazabicyclo[3,3,1]non-6-ene-6-carboxylic acid N-cyclopropyl-N-(3-methoxy-2-methylbenzyl)amide 881849-65-P, 7-[4-[N-(2,6-Dichlorobenzyl)-N-methylamino]methylphenyl]-3,9-diazabicyclo[3,3,1]non-6-ene-6-carboxylic acid N-cyclopropyl-N-(3-methoxy-2-methylbenzyl)amide 881849-66-7P, 7-[4-[N-(2,3-Difluorobenzyl)-N-methylamino]methyl]phenyl]-3,9-diazabicyclo[3,3,1]non-6-ene-6-carboxylic acid N-cyclopropyl-N-(3-methoxy-2-methylbenzyl)amide 881849-66-7P, 7-[4-[N-(2,3-Difluorobenzyl)-N-methylamino]methyl]phenyl]-3,9-diazabicyclo[3,3,1]non-6-ene-6-carboxylic acid N-cyclopropyl-N-(3-methoxy-2-methylbenzyl)amide 881849-66-7P, 7-[4-[N-(2,3-Difluorobenzyl)-N-(3-methoxy-2-methylbenzyl)amide 881849-66-7P, 7-[4-[N-(2,3-Difluorob

7-[4-[2-[N-(3-Chloro-2,6-difluorobenzyl)-N-cyclopropylamino]ethyl]phenyl
]-3,9-diazabicyclo[3.3.1]non-6-ene-6-carboxylic acid
N-cyclopropyl-N-[2,3dichlorobenzyl)amide 881849-68-9P, 7-[4-[[N-(3-Chloro-2-

dichlorobenzyl]amide 881849-68-9P, 7-[4-[[N-(3-Chloro-2-fluorobenzyl]-N-isopropylamino]methyl]phenyl]-3,9-diazabicyclo[3.3.1]non-6-ene-6-carboxylic acid N-cyclopropyl-N-(3-methoxy-2-methylbenzyl)amide 881849-69-0P, 7-[4-[[N-(3-Chloro-2,6-difluorobenzyl]-N-cyclopropylamio]methyl]phenyl]-3,9-diazabicyclo[3.3.1]non-6-ene-6-carboxylic acid N-cyclopropyl-N-(2,3-dichlorobenzyl)amide 881849-70-3P, 7-[4-[(N-cyclopropyl-N-(2,3-dichlorobenzyl)amide 881849-71-4P, 7-[4-[(N-cyclopropyl-N-(2,3-dichlorobenzyl)amide 881849-71-4P, 7-[4-[(N-cyclopropyl-N-(2,3-dichlorobenzyl)amide 881849-71-4P, 7-[4-[(N-cyclopropyl-N-(2,3-dichlorobenzyl)amide 881849-71-4P, 7-[4-[(N-cyclopropyl-N-(2,3-dichlorobenzyl)amide 881849-72-5P, 7-[4-[[N-cyclopropyl-N-(2,3-dichlorobenzyl)amide 881849-73-6P, 7-[4-[(N-cyclopropyl-N-(2,3-dichlorobenzyl)amide 881849-73-6P, 7-[4-[(N-cyclopropyl-N-(2,3-dichlorobenzyl)amide 881849-73-6P, 7-[4-[(N-cyclopropyl-N-(2,3-dichlorobenzyl)amide 881849-73-6P, 7-[4-[(N-cyclopropyl-N-(2,3-dichlorobenzyl)amide 681849-73-6P, 7-[4-[(N-cyclo

L4 ANSWER 7 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
881849-74-7P, 7-[4-[[N-(2-Cyanobenzyl)-Ncyclopropylamino]methyl]phenyl]-3,9-diazabicyclo[3,3,1]non-6-ene-6carboxylic acid N-cyclopropyl-N-(2,3-dichlorobenzyl)amide
881849-75-8P, 7-[4-[[N-(cyclopropyl-N-[quinolin-4yl]methyl]amino]methyl]phenyl]-3,9-diazabicyclo[3,3,1]non-6-ene-6carboxylic acid N-cyclopropyl-N-(2,3-dichlorobenzyl)amide
881849-76-9P, 7-[4-[[N-(6-Chloro-2-fluoro-3-methylbenzyl]-Ncyclopropylamino]methyl]phenyl]-3,9-diazabicyclo[3,3,1]non-6-ene-6carboxylic acid N-cyclopropyl-N-(2,3-dichlorobenzyl)amide
881849-77-0P, 7-[4-[[N-(cyclopropyl-N-(2-fluoro-6trifluoromethylbenzyl]amino]methyl]phenyl]-3,9-diazabicyclo[3,3,1]non-6ene-6-carboxylic acid N-cyclopropyl-N-(2,3-dichlorobenzyl)amide
881849-78-1P, 7-[4-[3-[N-(2-Fluoro-5-methylbenzyl]-Nmethylamino]propyl]-N-(3-methoxy-2-2-methylbenzyl)amide 881849-79-2P
, 7-[4-[3-[N-(2,3-Dichlorophenyl)-N-methylamino]propyl]phenyl]-3,9diazabicyclo[3,3,1]non-6-ene-6-carboxylic acid
N-cyclopropyl-N-(3-methoxy-2-2-methylbenzyl)amide 881849-79-2P

-2-methylbenzyl)amide 881849-80-5P, 7-[4-[3-[N-(2,6-

2-methylbenzyl) amide 881849-80-5P, 7-[4-[3-[N-{2,6Difluorophenyl]-N-methylamino]propyl]phenyl]-3,9-diazabicyclo[3.3.1]non-6.ene-6-carboxylic acid N-cyclopropyl-N-(3-methoxy-2-methylbenzyl)amide
881849-81-6P, 7-[4-[3-[N-(2,6-Dichlorophenyl]-Nmethylamino]propyl]phenyl]-3,9-diazabicyclo[3.3.1]non-6-ene-6-carboxylic
acid N-cyclopropyl-N-(3-methoxy-2-methylbenzyl)amide 881849-82-7P
, 7-[4-[3-[N-(2,5-Difluorophenyl]-N-methylamino]propyl]phenyl]-3,9diazabicyclo[3.3.1]non-6-ene-6-carboxylic acid
N-cyclopropyl-N-(3-methoxy2-methylbenzyl)amide 881849-83-8P, 7-[4-[3-[N-(5-Chloro-2methylphenzyl]-N-methylamino]propyl]phenyl]-3,9-diazabicyclo[3.3.1]non-6ene-6-carboxylic acid N-cyclopropyl-N-(3-methoxy-2-methylbenzyl)amide
881849-84-9P, 7-[4-[3-[N-(2,5-Dichlorophenzyl)-N-methylbenzyl)]ndiae
881849-84-9P, 7-[4-[3-[N-(2,5-Dichlorophenzyl)]-N-methylamino]propyl]phenyl]-3,9diazabicyclo[3.3.1]non-6-ene-6-carboxylic acid
N-cyclopropyl-N-(3-methoxy-2-methylbenzyl)amide 881849-85-0P
, 7-[4-[3-[N-(3-fluoro-2-methylphenzyl]-N-methylamino]propyl]phenyl]-3,9diazabicyclo[3.3.1]non-6-ene-6-carboxylic acid
N-cyclopropyl-N-(3-methoxy-2-methylphenzyl)-Nmethylphenzyl)amide 881849-86-1P, 7-[4-[3-[N-(5-Fluoro-2methylphenzyl])amide 881849-86-1P, 7-[4-[3-[N-(5-Fluoro-2methylphenzyl]-N-(3-methoxy-2-methylphenzyl)-Nmethylamino]propyl]phenyl]-3,9-diazabicyclo[3.3.1]non-6ene-6-carboxylic acid N-cyclopropyl-N-(3-methylphenzyl)amide 881849-88-3P
, 7-[4-[[N-(3-Chloro-2-6-difluorofenzyl]-N-(2,2,2trifluoroethyl)amino]methyl]phenyl]-3,9-diazabicyclo[3.3.1]non-6-ene-6carboxylic acid N-cyclopropyl-N-(2,3-dichlorobenzyl)amide
881849-89-89-7,7-[4-[(3-(3-chloro-2-fluoro-6-trifluoromethylbenzyl)-NC(2,2-trifluoroethyl)amino]methyl]phenyl]-3,9-diazabicyclo[3.3.1]non-6-ene-6carboxylic acid N-cyclopropyl-N-(2,3-dichlorobenzyl)amide
881849-89-89-7,7-[4-[(3-(3-chloro-2-fluoro-6-trifluoromethylbenzyl)-NC(2,2-trifluoroethyl)amino]methyl]phenyl]-3,9-diazabicyclo[3.3.1]non-6-ene-6carboxylic acid N-cyclopropyl-N-(2,3-dichlorobenzyl)a

N-(2,2,2-trifluoroethyl) amino]methyl]phenyl]-3,9-diazabicyclo[3.3.1]non-6-ene-6-carboxylic acid N-cyclopropyl-N-(2,3-dichlorobenzyl) amide 881849-90-7P, 7-[4-[N-3-Chloro-2-Tluorobenzyl]-N-i appropylamino]methyl]phenyl]-3,9-diazabicyclo[3.3.1]non-6-ene-6-carboxylic acid N-cyclopropyl-N-(2,3-dichlorobenzyl)amide RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(uses)
(prepn. of bicyclononene derivs. as inhibitors of renin for prophylaxis
or treatment of diseases related to the renin-angiotensin system)
RN 881849-16-7 CAPLUS

ANSWER 7 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

881849-20-3 CAPLUS
3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide, 7-[4-[3-[(2-chlorophenyl)methylamino]propyl]phenyl]-N-cyclopropyl-N-[(3-methoxy-2-methylphenyl)methyl]- (9CI) (CA INDEX NAME)

881849-21-4 CAPLUS
3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide, 7-[4-[3-[(3-chlorophenyl)methylamino]propyl]phenyl]-N-cyclopropyl-N-[(3-methoxy-2-methylphenyl)methyl]- (9CI) (CA INDEX NAME)

881849-22-5 CAPLUS
3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide, N-cyclopropyl-N-[(3-methoxy-2-methylphenyl)methyl]-7-[4-[2-(methylphenylamino)ethoxy]phenyl]-(9CI) (CA INDEX NAME)

ANSWER 7 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN (Continued) 3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide, N-cyclopropyl-7-[4-[3-[2,4-difluorophenyl]methylamino]propyl]phenyl]-N-[(3-methoxy-2-methylphenyl]methyl]- (9CI) (CA INDEX NAME)

881849-17-8 CAPLUS
3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide, N-cyclopropyl-N-[(3-methoxy-2-methylphenyl)methyl]-7-[4-[3-(methylphenylamino)propyl]phenyl]-(9CI) (CA INDEX NAME)

881849-18-9 CAPLUS
3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide, N-cyclopropyl-N-[(3-methoxy-2-methylphenyl)methyl]-7-[4-[3-[methyl]3-methylphenyl)amino]propyl)phenyl]- (9CI) (CA INDEX NAME)

881849-19-0 CAPLUS
3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide, N-cyclopropyl-N-[(3-methoxy-2-methylphenyl)methyl]-7-[4-[3-[methyl (2-methylphenyl)amino]propyl]phenyl]- (9CI) (CA INDEX NAME)

ANSWER 7 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN

881849-23-6 CAPLUS
3,9-Dlazabicyclo[3.3.1]non-6-ene-6-carboxamide, 7-[4-[2-{[3-chloro-2,6-df]lucroberzoyl]methylamino]ethyl]phenyl]-N-cyclopropyl-N-[(3-methoxy-2-methylphenyl)methyl]- (9CI) (CA INDEX NAME)

3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide, N-cyclopropyl-7-[4-[2-[[(4,5-dichloro-3-isothiazolyl]carbonyl]methylaminojethy]phenyl]-N-[(3-methoxy-2-methylphenyl]methyl]- [9CI] (CA INDEX NAME)

RN 881849-25-8 CAPLUS
CN 3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide,
N-cyclopropyl-7-[4-[[[2.4dichloropheny1]methyl]methylamino]methyl]phenyl]-N-[{3-methoxy-2methylphenyl}methyl]- (9CI) (CA INDEX NAME)

RN 881849-26-9 CAPLUS
CN 3,9-blazableyclo[3.3.1]non-6-ene-6-carboxamide,
7-[4-[[[2-chloro-6-fluoro3-methylphenyl]methyl]methylamino[methyl]phenyl]-N-cyclopropyl-N-[(3-methyv)-2-methylphenyl]methyl]- (9CI) (CA INDEX NAME)

881849-27-0 CAPLUS
3,9-Diazabicyclo(3.3.1]non-6-ene-6-carboxamide, 7-[4-[[[(2-chloro-3,6-difluorophenyl)methyl]methylamino|methyl]phenyl}-N-cyclopropyl-N-[(3-methoxy-2-methylphenyl)methyl]- (9CI) (CA INDEX NAME)

881849-28-1 CAPLUS 3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide, 7-[4-[[[(2-chloro-4-

fluorophenyl)methyl]methylamino]methyl]phenyl]-N-cyclopropyl-N-[(3-methoxy-2-methylphenyl)methyl]- (9CI) (CA INDEX NAME)

ANSWER 7 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN

881849-32-7 CAPLUS
3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide,
clopropyl-7-[4-[[[(2,6dichlorophenyl]methyl]methylamino]methyl]phenyl]-N-[(3-methoxy-2methylphenyl)methyl]- (9CI) (CA INDEX NAME)

881849-33-8 CAPLUS 3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide, 7-[4-{2-[[{2-chloro-6-

fluoro-3-methylphenyl)methyl]methylamino]ethyl]phenyl]-N-cyclopropyl-N-[(3-methoxy-2-methylphenyl)methyl]- (9CI) (CA INDEX NAME)

881849-34-9 CAPLUS
3,9-Diazabicyclo[3,3.1]non-6-ene-6-carboxamide, 7-[4-[2-[[(2-chloro-3,6-difluorophenyl)methyl]methylamino]ethyl]phenyl]-N-cyclopropyl-N-[(3-methoxy-2-methylphenyl)methyl]- (9CI) (CA INDEX-NAME)

ANSWER 7 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN

881849-29-2 CAPLUS
3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide, 7-{4-{{[(2-chloro-6-

fluorophenyl)methyl]methylamino]methyl]phenyl]-N-cyclopropyl-N-{(3-methoxy-2-methylphenyl]methyl]- (9CI) (CA INDEX NAME)

RN 881849-30-5 CAPLUS
CN 3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide,
N-cyclopropyl-7-[4-[[[(2,3dichlorophenyl]methyl]methylamino]methyl]phenyl]-N-[(3-methoxy-2methylphenyl)methyl]- (9CI) (CA INDEX NAME)

881849-31-6 CAPLUS 3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide, 7-{4-[[[(2-

chlorophenyl)methyl]methylamino]methyl]phenyl]-N-cyclopropyl-N-[(3-methoxy-2-methylphenyl)methyl]- (9CI) (CA INDEX NAME)

ANSWER 7 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN

881849-35-0 CAPLUS
3,9-Diazabicyclo{3.3.1}non-6-ene-6-carboxamide, 7-{4-[2-[{{2-chloro-6-

fluorophenyl)methyl]methylamino|ethyl]phenyl]-N-cyclopropyl-N-[(3-methoxy-2-methylphenyl)methyl]- (9CI) (CA INDEX NAME)

881849-36-1 CAPLUS
3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide, N-cyclopropyl-7-[4-[2-[(2,3-d-(th.Orophenyl)methyl]methylamino]ethyl]phenyl]-N-[(3-methoxy-2-methylphenyl)methyl]- (9CI) (CA INDEX NAME)

881849-37-2 CAPLUS
3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide, 7-[4-[2-[[{2-

chlorophenyl)methyl]methylamino]ethyl]phenyl]-N-cyclopropyl-N-[(3-methoxy-2-methylphenyl)methyl]- (9CI) (CA INDEX NAME)

881849-39-4 CAPLUS
3,9-Dlazabicyclo[3.3.1]non-6-ene-6-carboxamide, N-cyclopropyl-7-[4-[2-[[2,6-dichlorophenyl]methyl]methylamino]ethyl]phenyl]-N-[[3-methoxy-2-methylphenyl]methyl]- (9CI) (CA INDEX NAME)

(Continued)

881849-40-7 CAPLUS
3,9-Diazabicyclo[3,3,1]non-6-ene-6-carboxamide, N-cyclopropyl-7-[4-[[2-(2,4-dimethylphenoxy)ethyl]methylamino]methyl]phenyl]-N-[(3-methoxy-2-methylphenyl)methyl]- (9CI) (CA INDEX NAME)

RN 881849-41-8 CAPLUS
CN 3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide,
N-cyclopropyl-7-[4-[[[(2,6-

dichloro-4-methylphenyl)methyl]methylamino]methyl]phenyl]-N-[(3-methoxy-2-methylphenyl)methyl]- (9CI) (CA INDEX NAME)

ANSWER 7 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN

881849-45-2 CAPLUS
3,9-Diazabicyclo(3.3.1]non-6-ene-6-carboxamide, N-cyclopropyl-7-[4-[2-[(2,6-dimethylphenyl)methyl]methyl]methylamino]ethyl]phenyl]-N-[(3-methoxy-2-methylphenyl)methyl]- (9CI) (CA INDEX NAME)

881849-46-3 CAPLUS :
3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide, N-cyclopropyl-N-[(3-methoxy-2-methylphenyl)methyl]-7-[4-[2-[methyl](2,3,6-trichlorophenyl)methyl]amino]ethyl]phenyl]- (9CI) (CA INDEX NAME)

881849-47-4 CAPLUS
3,9-Diazabicyclo[3,3.1]non-6-ene-6-carboxamide, N-cyclopropyl-N-[(3-methoxy2-methylphenyl)methyl]-7-[4-{[methyl[(2,3,6-trichlorophenyl]methyl]amino]methyl]phenyl]- (9CI) (CA INDEX NAME)

881849-42-9 CAPLUS
3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide, 7-[4-[[[(2-chlorophenyl]methyl]cyclopropylamino]methyl]phenyl]-N-cyclopropyl-N-[(3-methoxy-2-methylphenyl)methyl]- (9CI) (CA INDEX NAME)

881849-43-0 CAPLUS
3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide, N-cyclopropyl-N-[(3-methoxy-2-methylphenyl)methyl]-7-[4-[[methyl[2-(2,3,6-trichlorophenyl)ethyl]amino]methyl]phenyl] (9CI) (CA INDEX NAME)

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881849-44-1 CAPLUS
3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide, 7-[4-[2-[[(3-

chlorophenyl)methyl]methylamino]ethyl]phenyl]-N-cyclopropyl-N-[(3-methoxy-2-methylphenyl)methyl]- (9CI) (CA INDEX NAME)

ANSWER 7 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN

881849-48-5 CAPLUS
3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide, 7-[4-[[[(3-chloro-2,6-difluorophenyl)methyl]ethylamino]methyl]phenyl]-N-cyclopropyl-N-[(2,3-dichlorophenyl)methyl]- (9CI) (CA INDEX NAME)

881849-49-6 CAPLUS
3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide, 7-[4-[[[3-chlorophenyl]methyl]ethylamino]methyl]phenyl]-N-cyclopropyl-N-[(2,3-dichlorophenyl)methyl]- (9CI) (CA INDEX NAME)

881849-50-9 CAPLUS 3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide, N-cyclopropyl-N-[(2,3-

881849-51-0 CAPLUS 3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide, N-cyclopropyl-N-[{2,3-

(Continued)

881849-52-1 CAPLUS
3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide, 7-[4-[[[(2-chloro-3,6-difluorophenyl)methyl]ethylamino]methyl]phenyl]-N-cyclopropyl-N-[(2,3-dichlorophenyl)methyl]- (9CI) (CA INDEX NAME)

881849-53-2 CAPLUS 3,9-Diazabicyclo(3.3.1]non-6-ene-6-carboxamide, N-cyclopropyl-N-[{2,3-dichlorophenyl)methyl]-7-[4-[[([2,2-difluoro-1,3-benzodioxol-4-yl)methyl]ethylamino]methyl]phenyl]- (9CI) (CA INDEX NAME)

ANSWER 7 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN (Continued) 3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide, N-cyclopropyl-N-{(2,3dichlorophenyl)methyl]-7-[4-[[(2,6-difluorophenyl)methyl]ethylamino]methyl]phenyl]- (9CI) (CA INDEX NAME) .

881849-57-6 CAPLUS
3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide, N-cyclopropyl-N-[(2,3-

RN 881849-58-7 CAPLUS
CN 3,9-Diazabicyclo[3,3.1]non-6-ene-6-carboxamide,
7-[4-[[[2-chloro-6-fluoro3-methylphenyl]methyl]ethylamino]methyl]phenyl]-N-cyclopropyl-N-[[2,3dichlorophenyl]methyl]- (9CI) (CA INDEX NAME)

881849-59-8 CAPLUS
3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide, N-cyclopropyl-N-[(2,3dichlorophenyl)methyl]-7-[4-[[[{2,4-dichlorophenyl)methyl]ethylamino]methy

881849-54-3 CAPLUS 3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide, N-cyclopropyl-N-[$\{2,3-1\}$]

881849-55-4 CAPLUS 3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide, 7-[4-[[[(2-cyanophenyl]methyl]ethylamino]methyl]phenyl]-N-cyclopropyl-N-[(2,3-dichlorophenyl)methyl]- (9CI) (CA INDEX NAME)

881849-56-5 CAPLUS

ANSWER 7 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN l]phenyl]- (9CI) (CA INDEX NAME)

881849-60-1 CAPLUS
3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide, 7-[4-[[(2-chloro-6-fluorophenyl)methyl]ethylamino]methyl]phenyl]-N-cyclopropyl-N-[(2,3-dichlorophenyl)methyl]- (9CI) (CA INDEX NAME)

881849-61-2 CAPLUS
3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide, N-cyclopropyl-N-[(2,3-dichlorophenyl)methyl]-7-[4-[[ethyl((2-fluoro-5-methoxyphenyl)methyl]amino[methyl]phenyl]- (9CI) (CA INDEX NAME)

881849-62-3 CAPLUS
3,9-Dlazabitcyclo[3.3.1]non-6-ene-6-carboxamide, N-cyclopropyl-N-{{2,3-dichlorophenyl)methyl}-7-{4-{[ethyl]{2-fluoro-6-(trifluoromethyl)phenyl]methyl}amino]methyl]phenyl}- (9CI) (CA INDEX NAME)

881849-63-4 CAPLUS
3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide, N-cyclopropyl-N-[(2,3-

RN 881849-64-5 CAPLUS
CN 3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide,
N-cyclopropyl-7-14-[[[(2,6dimethylphenyl]methyl]methylamino]methyl]phenyl]-N-{(3-methoxy-2methylphenyl)methyl]- (9CI) (CA INDEX NAME)

RN 881849-65-6 CAPLUS
CN 3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide,
7-[4-[[[6-chloro-2-fluoro3-methylphenyl]methyl]methylamino]methyl]phenyl]-N-cyclopropyl-N-[(3-methylphenyl)phenyl]methyl]-[9CI] (CA INDEX NAME)

ANSWER 7 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN

881849-69-0 CAPLUS
3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide, 7-[4-[{[(3-chloro-2,6-difluorophenyl)methyl]cyclopropylamino]methyl]phenyl]-N-cyclopropyl-N-[(2,3-dichlorophenyl)methyl]- (9CI) (CA INDEX NAME)

881849-70-3 CAPLUS
3,9-Diazabicyclo(3.3.1]non-6-ene-6-carboxamide, N-cyclopropyl-7-{4-[cyclopropyl[(2,6-dichlorophenyl]methyl]amino|methyl]phenyl]-N-[(2,3-dichlorophenyl)methyl]- (9CI) (CA INDEX NAME)

881849-71-4 CAPLUS
3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide, N-cyclopropyl-7-[4-[cyclopropyl[(2,3-dichlorophenyl)methyl]amino]methyl]phenyl]-N-[(2,3-dichlorophenyl)methyl]- (9CI) (CA INDEX NAME)

RN 881849-66-7 CAPLUS
CN 3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide,
N-cyclopropyl-7-[4-[[[2,3difluorophenyl]methyl]methylamino]methyl]phenyl]-N-[[3-methoxy-2methylphenyl]methyl]- (9CI) (CA INDEX NAME)

881849-67-8 CAPLUS 3,9-Diazabicyclo(3.3.1)non-6-ene-6-carboxamide, 7-[4-[2-{[(3-chloro-2,6-

difluorophenyl)methyl]cyclopropylamino]ethyl]phenyl]-N-cyclopropyl-N-[{2,3-dichlorophenyl)methyl}- (9CI) (CA INDEX NAME)

881849-68-9 CAPLUS
3,9-Diazabicyclo[3,3.1]non-6-ene-6-carboxamide, 7-[4-[[[(3-chloro-2-fluoropheny1)methyl](1-methylethyl)amino]methyl]phenyl]-N-cyclopropyl-N-[(3-methoxy-2-methylphenyl)methyl]- [9C1] (CA INDEX NAME)

ANSWER 7 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

881849-72-5 CAPLUS
3,9-Dlazabicyclo[3.3.1]non-6-ene-6-carboxamide, N-cyclopropyl-7-[4-[[cyclopropyl[(2,3,6-trichlorophenyl)methyl]amino]methyl]phenyl]-N-[(2,3-dichlorophenyl)methyl]- (9CI) (CA INDEX NAME)

3,9-Digazbicyclo[3.3.1]non-6-ene-6-carboxamide, N-cyclopropyl-7-[4-[[cyclopropyl]c(5-dimethylphenyl)methyl]amino|methyl|phenyl]-N-[(2,3-dichlorophenyl)methyl]- (CG INDEX NAME)

881849-74-7 CAPLUS
3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide, 7-[4-[[[2-cyanophenyl]methyl]cyclopropylamino]methyl]phenyl]-N-cyclopropyl-N-[(2,3-dichlorophenyl)methyl]- (9CI) (CA INDEX NAME)

881849-75-8 CAPLUS
3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide, N-cyclopropyl-7-[4-[(cyclopropyl(4-quinolinylmethyl)amino]methyl]phenyl]-N-[(2,3-dichlorophenyl)methyl]- (9CI) (CA INDEX NAME)

(Continued)

RN 881849-76-9 CAPLUS
CN 3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide,
7-[4-[[[(6-chloro-2-fluoro3-methylphenyl]methyl]cyclopropylamino]methyl]phenyl)-N-cyclopropyl-N(2,3-dichlorophenyl)methyl]- (9CI) (CA INDEX NAME)

ANSWER 7 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN

881849-80-5 CAPLUS
3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide, N-cyclopropyl-7-[4-[3-(2,6-difluorophenyl)methylamino]propyl]phenyl]-N-[[3-methoxy-2-methylphenyl)methyl]- (9CI) (CA INDEX NAME)

881849-81-6 CAPLUS
3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide, N-cyclopropyl-7-[4-[3-[(2,6-dichlorophenyl)]methylamino]propyl]phenyl]-N-[(3-methoxy-2-methylphenyl)methyl]- (9CI) (CA INDEX NAME)

881849-82-7 CAPLUS
3,9-Diazabicyclo(3.3.1]non-6-ene-6-carboxamide, N-cyclopropyl-7-{4-{3-[(2,5-difluorophenyl)methylamino]propyl]phenyl]-N-[(3-methoxy-2-methylphenyl)methyl]- (9CI) (CA INDEX NAME)

881849-77-0 CAPLUS 3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide, N-cyclopropyl-7-[4-

[[cyclopropy1[[2-fluoro-6-(trifluoromethy1)pheny1]methy1]amino]methy1]phen y1]-N-[(2,3-dichloropheny1)methy1]- (9CI) (CA INDEX NAME)

RN 881849-78-1 CAPLUS
CN 3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide,
N-cyclopropyl-7-[4-[3-[(2fluoro-5-methylphenyl]methylamino]propyl]phenyl]-N-[(3-methoxy-2methylphenyl)methyl]- (9CI) (CA INDEX NAME)

881849-79-2 CAPLUS
3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide, N-cyclopropyl-7-[4-[3-[(2,3-dichorophenyl)methylamino]propyl]phenyl]-N-[(3-methoxy-2-methylphenyl)methyl]- (9CI) (CA INDEX NAME)

ANSWER 7 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN

881849-83-8 CAPLUS
3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide, 7-[4-[3-[(5-chloro-2-methylphenyl)methylamino]propyl]phenyl]-N-cyclopropyl-N-[(3-methoxy-2-methylphenyl)methyl]- (9CI) (CA INDEX NAME)

881849-84-9 CAPLUS 3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide, N-cyclopropyl-7-[4-[3-[(2,5-dichlorophenyl)methylamino]propyl]phenyl]-N-[(3-methoxy-2-methylphenyl)methyl]- (9CI) (CA INDEX NAME)

881849-85-0 CAPLUS
3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide,
yclopropyl-7-[4-[3-[(3fluoro-2-methylphenyl)methylamino]propyl]phenyl]-N-[(3-methoxy-2methylphenyl)methyl]- (9CI) (CA INDEX NAME)

(Continued)

RN 881849-86-1 CAPLUS
CN 3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide,
N-cyclopropyl-7-(4-[3-[65fluoro-2-methylphenyl]methylamino]propyl]phenyl]-N-[(3-methoxy-2methylphenyl)methyl]- (9CI) (CA INDEX NAME)

881849-87-2 CAPLUS
3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide, 7-[4-[3-[(2-chloro-5-methylphenyl)methyl]amtno[propyl]phenyl]-N-cyclopropyl-N-[(3-methoxy-2-methylphenyl)methyl]- (9CI) (CA INDEX NAME)

881849-88-3 CAPLUS
3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide, 7-[4-[[[(3-chloro-2,6-difluorophenyl)methyl]-N-cyclopropyl-N-[(2,3-dichlorophenyl)methyl]-(9CI) (CA INDEX NAME)

L4 ANSWER 8 0F 15 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:193834 CAPLUS
DOCUMENT NUMBER: 144:274301
TITLE: 14:274301
Preparation of diazabicyclononenylacetamides as renin inhibitors.

INVENTOR(S):

inhibitors.

Bezencon, Olivier; Boss, Christoph; Bur, Daniel;
Corminboeuf, Olivier; Fischli, Walter; Grisostomi,
Corinna; Remen, Lubos; Richard, Sylvia; Sifferlen,
Thierry; Weller, Thomas
Actelion Pharmaceuticals Ltd, Switz.
PCT Int. Appl., 46 pp.
CODEN: PIXXD2
Patent
English

PATENT ASSIGNEE(S): SOURCE:

DOCUMENT TYPE:

FAMILY ACC. NUM. COUNT: PATENT INFORMATION:

| WO 2005-EP9050 | 20050822 |
|--------------------------|---|
| | 20050822 |
| | |
| I, BB, BG, BK, BW, BY, I | BZ, CA, CH, |
| , DZ, EC, EE, EG, ES, I | FI, GB, GD, |
| , IS, JP, KE, KG, KM, I | KP, KR, KZ, |
| , MD, MG, MK, MN, MW, 1 | MX, MZ, NA, |
| , PT, RO, RU, SC, SD, S | SE, SG, SK, |
| , TZ, UA, UG, US, UZ, 1 | VC, VN, YU, |
| | |
| C, EE, ES, FI, FR, GB, C | GR, HU, IE, |
| , PT, RO, SE, SI, SK, | TR, BF, BJ, |
| , ML, MR, NE, SN, TD, | TG, BW, GH, |
| , SZ, TZ, UG, ZM, ZW, J | AM, AZ, BY, |
| | |
| | N, BB, BG, BR, BW, BY, 16, DZ, EC, EE, EG, ES, 1, IS, JP, KE, KG, KM, MD, MG, MK, MN, MW, PT, RO, RU, SC, JUA, UG, US, UZ, C, EE, ES, FI, FR, GB, PT, RO, SE, SI, SK, ML, MR, NE, NN, TD, ML, MR, NE, NN, TD, ML, MR, NE, NN, TD, ND, ND, ND, ND, ND, ND, ND, ND, ND, N |

GM, KE, LS, KG, KZ, MD, PRIORITY APPLN. INFO.:

OTHER SOURCE(S):

MARPAT 144:274301

Title compds. (I; Z = NH, NL, CH2, CHL, O, S; W = Ph substituted by V in para position; V = oxyalkylene, oxyalkyleneoxy; U = (substituted) aryl;

Y = bond, alkylene; Q = CONR1; M = (substituted) Ph, pyridyl; L = R3, COR3, COR3, CONR2R3, SO2R3, SO2NR2R3; R1 = alkyl, cycloalkyl; R2 = H, alkyl, alkenyl, cycloalkyl, cycloalkylakyl; R3 = (substituted) alkyl, cycloalkyl, cycloalkylakyl; R3 = (substituted) alkyl, cycloalkyl, cycloalkylakyl; with a proviso], were prepared Thus,

nic
N-(2-chlorobenzyl)-2-[(1R*,5S*,6R*)-7-[4-[3-(2-chloro-3,6difluorophenoxy)propyl]phenyl]-3,9-diazabicyclo(3.3.1)non-7-en-6-yl]-Ncyclopropylacetamide (multistep preparation given) inhibited renin with IC50

1.4 nM. 877995-55-6P 877995-56-7P 877995-57-8P 877995-58-9P 877995-60-3P 877995-62-5P

F3C-CH2

RN 881849-89-4 CAPLUS
CN 3,9-Diazabicyclo(3.3.1)non-6-ene-6-carboxamide,
7-[4-[[[3-chloro-2-fluoro-

6-(trifluoromethyl)phenyl]methyl]{2,2,2-trifluoroethyl}amino]methyl]phenyl }-N-cyclopropyl-N-[{2,3-dichlorophenyl}methyl]- {9CI} (CA INDEX NAME}

881849-90-7 CAPLUS
3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide, 7-[4-[[[(3-chloro-2-fluorophenyl)methyl](1-methylethyl)amino]methyl]phenyl]-N-cyclopropyl-N-[(2,3-dichlorophenyl)methyl]- (9CI) (CA INDEX NAME)

ANSWER 8 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN (Continued) 877995-64-7P 877995-66-9P 877995-67-0P 877995-92-9 877995-71-6F RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(Uses)
(claimed compd.; prepn. of diazabicyclononenylacetamides as renin inhibitors)
8.77995-55-6 CAPLUS
3,9-Diazabicyclo[3.3.1]non-7-ene-6-acetamide, 7-[4-[3-(2-chloro-3,6-difluorophenoxy)]ropyl]phenyl]-N--((2-chlorophenyl)methyl]-N-cyclopropyl-, (1R,5S,6R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

877995-56-7 CAPLUS
3,9-Diazabicyclo[3.3.1]non-7-ene-6-acetamide, 7-[4-[3-(2-chloro-3,6-difluorophenoxy]propyl]phenyl]-N-cyclopropyl-N-[(2-fluoro-5-methoxyphenyl)methyl]-, (1R,5S,6R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

(Continued)

877995-57-8 CAPLUS
3,9-Diazabicyclo{3.3.1}non-7-ene-6-acetamide, 7-[4-[3-(2-chloro-3,6-difluorophenoxy)propyl]phenyl}-N-cyclopropyl-N-[(3-methoxy-2-methylphenyl)methyl}-, {1R,55,6R}-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

877995-58-9 CAPLUS
3,9-Diazabicyclo[3.3.1]non-7-ene-6-acetamide, 7-[4-[3-(2-chloro-3,6-difluorophenoxy]propyl]phenyl]-N-cyclopropyl-N-[(2-methoxy-3-methyl-4-pyridinyl]methyl)-, (IR,55,6R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

ANSWER 8 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN

877995-64-7 CAPLUS
3,9-Diazabicyclo[3.3.1]non-7-ene-6-acetamide, 7-[4-[3-{2-chloro-3,6-difluorophenoxy)propyl]phenyl]-N-cyclopropyl-N-[(2,3-dimethylphenyl)methyl]-, (1R,5S,6R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

RN 877995-66-9 CAPLUS
CN 3,9-blezabicyclo[3.3.1]non-7-ene-6-acetamide, 7-[4-(3-(2-chloro-3,6-difluorophenoxy)propyl]phenyl]-N-methyl-N-(phenylmethyl)-,
(LR,S5,6R)-rel(SCI) (CA INDEX NAME)

Relative stereochemistry.

L4 ANSWER 8 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN

877995-60-3 CAPLUS 3,9-Diazabicyclo[3.3.1]non-7-ene-6-acetamide, 7-[4-[3-{2-chloro-3,6difluorophenoxy)propyl]phenyl]-N-cyclopropyl-N-[(3-methoxyphenyl)methyl]-, (1R,5S,6R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

877995-62-5 CAPLUS 3,9-Diazabicyclo[3,3.1]non-7-ene-6-acetamide, 7-{4-[3-(2-chloro-3,6-difluorophenoxy)propyl]phenyl}-N-cyclopropyl-N-[(2,3-dichlorophenyl)methyl]-, (1R,5S,6R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

L4 ANSWER 8 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN · (Continued)

877995-67-0 CAPLUS
3,9-Diazabicyclo[3,3.1]non-7-ene-6-acetamide, 7-{4-[3-{2-chloro-3,6-difluorophenoxy)propyl]phenyl]-N-[{2-chlorophenyl}methyl}-N-ethyl-,(1R,5S,68)-rel- [9CI) (CA INDEX NAME)

Relative stereochemistry.

877995-69-2 CAPLUS
3,9-Diazabicyclo[3.3.1]non-7-ene-6-acetamide, 7-{4-(3-{2-chloro-3,6-difluorophenoxy}propyl]phenyl}-N-cyclopropyl-N-{{3,5-dimethoxyphenyl}methyl}-, (1R,5s,6R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

877995-71-6 CAPLUS 3,9-Diazabicyclo[3,3.1]non-7-ene-6-acetamide, 7-[4-[3-(2-chloro-3,6-difluorophenoxy)propyl]phenyl]-N-cyclopropyl-N-[(3,4-dimethoxyphenyl)methyl]-, (1R,55,68)-rel- (9CI) (CA INDEX NAME) RN CN

Relative stereochemistry.

877996-05-9P 877996-06-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological atudy); PREP (Preparation); USES (Uses) (preparation of diazabicyclononenylacetamides as renin inhibitors) 877996-05-9 CAPLUS
3,9-Diazabicyclo[3.3.1]non-7-ene-6-acetamide, 7-[4-[3-(2-chloro-3,6-difluorophenoxy)]propyl]phenyl]-N-cyclopropyl-N-[(3-methoxy-2-methylphenyl)]-, monohydrochloride, (1R,58,6R)-rel- (9CI) (CA

ANSWER 8 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN

ANSWER 8 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN NAME)

● HC1

877996-06-0 ·CAPLUS 3,9-Diazabicyclo[3.3.1]non-7-ene-6-acetamide, 7-[4-[3-(2-chloro-3,6-difluorophenoxy)propyl]phenyl]-N-cyclopropyl-N-[(2-methoxy-3-methyl-4-pyridinyl)methyl]-, monohydrochloride, (1R,5S,6R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

REFERENCE COUNT:

THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L4 ANSWER 9 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:193413 CAPLUS
DOCUMENT NUMBER: 144:274299
TITLE: Preparation of diazabicylononenes as renin
inhibitors.
INVENTOR(S): Bezencon, Olivier; Boas, Christoph, Bur, De

Bezencon, Olivier; Boss, Christoph; Bur, Daniel; Corminboeuf, Olivier; Fischli, Walter; Grisostomi, Corinns; Remen, Lubos; Richard, Sylvie; Sifferlen, Thierry; Weller, Thomas Actelion Pharmaceuticals Ltd., Switz. PCT Int. Appl., 98 pp. CODEN: PIXXD2 Patent English 1

PATENT ASSIGNEE(S): SOURCE:

DOCUMENT TYPE: LANGUAGE: FAMILY ACC. NUM. COUNT: PATENT INFORMATION:

PATENT NO: KIND DATE APPLICATION NO. DATE A2 20060302 A3 20060413 AM, AT, AU, AZ, BA, CU, CZ, DE, DK, DM, HR, HU, ID, II, IN, LS, LT, LU, LV, MA, NZ, OM, PG, PH, PL, TJ, TM, TN, TR, TT, WO 2005-EP9048 20050822 BB, DZ, IS, MD, PT, BG, BR, BW, EC, EE, EG, JP, KE, KG, MG, MK, MN, RO, RU, SC, UA, UG, US, BY, ES, KM, MW, SD, UZ, BZ, FI, KP, MX, SE, VC, CA, CH, GB, GD, KR, KZ, MZ, NA, AL, CR, GM, LR, NO, SY, ZW BG, LT, CI, LS, MD, CH, CY, CZ, DE, DK, EE, ES, LU, LV, MC, NL, PL, PT, RO, CM, GA, GN, GQ, GW, ML, MR, MW, MZ, NA, SD, SL, SZ, TZ, RU, TJ, TM FI, FR, SE, SI, NE, SN, UG, ZM, GB, GR, HU, IE, SK, TR, BF, BJ, TD, TG, BW, GH, ZW, AM, AZ, BY, PRIORITY APPLN. INFO.: A 20040825

OTHER SOURCE(S):

CASREACT 144:274299; MARPAT 144:274299

AB

U = (substituted) aryl, 5-membered heteroaryl; T = CONR1; Q = CH2; M = (substituted) Ph, pyridyl; L = R3, COR3, CO2R3, CONR2R3, SO2R3, SO2NR2R3; R1 = aikyl, cycloaikyl; R2 = (H, eikyl, alkenyl, cycloaikyl, cycloaikyl; R3 = (substituted) aikyl, cycloaikyl, cycloaikylakyl; with a proviso], were prepared Thus, (IRS, 5SR)-7-(4-(1GR)-3-(2,6-dichloro-4-methylphenoxylpyrrolidin-1-yl]phenyl)-3,9-diazabicyclo[3.3.1]non-6-ene-6-carboxylic acid cyclopropyl(3-methoxy-2-methylbenzyl)anide (multistep preparation given) inhibited renin with ICSO = 1.1 nM.

IT 878012-13-6P 878012-14-7P 878012-12-7P 878012-12-2P 878012-16-9P 878012-17-0P 878012-27-2P

ANSWER 9 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN (Continued) RL: PAC (Pharmacological activity); SPN (Synthetic preparation); TUU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(Uses)
(claimed compd.; prepn. of diazabicylononenes as renin inhibitors)
878012-13-6 CAPLUS
3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide, N-cyclopropyl-N-[(3-methoxy2-e-methylphenyl)methyl]-7-[4-[(38)-3-(2,3,6-trifluorophenoxy)-1-pyrrolidinyl]methyl)phenyl)- (9CI) (CA INDEX NAME)

RN 878012-14-7 CAPLUS
CN 3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide,
N-cyclopropyl-7-[4-[(138)3-(2,6-dichlorophenoxy)-1-pyrrolidinyl]methyl]phenyl]-N-[(3-methoxy-2-methylphenyl)methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 878012-15-8 CAPLUS
CN 3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide,
N-cyclopropyl-7-[4-[[(38)3-(2,6-dichloro-4-fluorophenoxy)-1-pyrrolidinyl]methyl]phenyl]-N-[(3-methoxy-2-methylphenyl)methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

ANSWER 9 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 878012-27-2 CAPLUS
CN 3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide,
N-cyclopropyl-7-[4-[{|3R|}-3-(2,3-difluorophenoxy)-1-pyrrolidinyl]methyl]phenyl]-N-[{3-methoxy-2-methylphenyl}methyl]- (9CI) (CA INDEX NAME)

878013-39-9P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES IT

(preparation of diazabicylononenes as renin inhibitors)
RN 878013-39-9 CAPLUS
CN 3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide,
7-[4-[[(33)-3-[2-chloro-6-

fluoro-3-methylphenoxy)-1-pyrrolidinyl]methyl]phenyl]-N-cyclopropyl-N-[(3-methoxy-2-methylphenyl)methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

ANSWER 9 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

878012-16-9 CAPLUS
3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide, 7-{4-{[(3S)-3-(2-chloro-3,6-difluorophenoxy)-1-pyrrolidinyl]methyl]phenyl]-N-cyclopropyl-N-[(3-methoxy-2-methylphenyl)methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 878012-17-0 CAPLUS
CN 3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide,
7-[4-[[(3R)-3-(2-chloro-6-

fluoro-3-methylphenoxy)-1-pyrrolidinyl]methyl]phenyl]-N-cyclopropyl-N-[(3-methoxy-2-methylphenyl)methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

ANSWER 9 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN

L4 ANSWER 10 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:523456 CAPLUS
DOCUMENT NUMBER: 143:60005
TITLE: Paperation of diazabicyclononene derivatives and their use as renin inhibitors
INVENTOR(S): Bezencon, Olivier; Richard-Bildstein, Sylvia; Bur, Daniel; Fischli, Walter; Weller, Thomas; Remen,

Sifferlen, Thierry Actelion Pharmaceuticals Ltd., Switz. PCT Int. Appl., 42 pp. CODEN: PIXXD2 PATENT ASSIGNEE(S): SOURCE:

DOCUMENT TYPE: Patent English 1

FAMILY ACC. NUM. COUNT: PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE WO 2005054243 Al 20050616 W0 2004-EP13578 2,
AM, AT, AU, AZ, BA, BB, BB, BG, BR, BW, BY,
CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI,
HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR,
IT, LU, LV, HA, MD, MG, MK, MN, MM, MX,
PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK,
TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, AK,
KE, LS, MW, MX, NA, SD, SL, SZ, TZ, UG, ZM,
KE, LS, MW, MX, NA, SD, SL, SZ, TZ, UG, ZM,
KE, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CA,
FR, GB, GR, HU, IE, IS, IT, IU, MC, NL, PL,
TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW,
TG
Al 20050616 AU 2004-295091 22
Al 20050616 CA 2004-2547547 Al 20050623 EP 2004-619638
DE, DK, ES, FR, GB, GR, TT, II, IU, NL, SE,
DE, DK, ES, FR, GB, GR, TT, II, IU, NL, SE,
DE, DK, ES, FR, GB, GR, TT, II, IU, NL, SE, 2005054243
W: AE, AG, AL,
CN, CO, CR,
GE, GH, GM,
LK, LR, LS,
NO, NZ, OM,
TJ, TM, TN,
RW: BW, GH, GM,
AZ, BY, KG,
EE, ES, FI,
SE, SI, SK,
NE, SN, TD,
2004295091 Al 20050616 WO 2004-EP13578 20041130 BZ, CA, CH, FI, GB, GD, KR, KZ, LC, FI, GB, GD, KR, KZ, LC, MZ, NA, NI, SK, SL, SY, ZA, ZM, ZW ZM, ZW, AM, CZ, DE, DK, PL, PT, RO, GW, ML, MR, NE, SN, TD,
AU 2004295091
CA 2547547
EP 1692133
R: AT, BE, CH,
IE, SI, FI,
CN 1890240
JP 2007513106
US 2007111989
IN 2006CN02464
PRIORITY APPIN. INFO:: AU 2004-25091 CA 2004-2547547 EP 2004-819638 GB, GR, IT, LI, LU, CZ, EE, HU, PL, SK, CN 2004-80035994 JP 2006-541864 US 2006-581829 IN 2006-CN2464 WO 2003-EP313767 20050616 20050616 20060823 , ES, FR, TR, BG, 20070103 20070524 20070517 20070608 20041130 20041130 20041130 SE, MC, PT, Al DE, DK, RO, CY, A T Al A 20041130 20041130 20060602 20060705 20031205 WO 2004-EP13578 W 20041130

OTHER SOURCE(S):

MARPAT 143:60005

Novel 3,9-diazabicyclo[3.3.1] nonene derivs. of formula (I) [X, W = N, CH; AB

ANSWER 10 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN

854053-00-2 CAPLUS
3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide, 7-[4-[3-(2-chloro-3,6-difluorophenoxy)propyl]phenyl]-N-cyclopropyl-N-[[3-(2-methoxyethoxy)-2-methylphenyl]methyl]- (9CI) (CA INDEX NAME)

REFERENCE COUNT:

THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

ANSWER 10 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN (Continued) V = (CH2)r, A-(CH2)s, CH2-A-(CH2)t, (CH2)s-A, (CH2)2-A-(CH2)u,

(CH2)3-A-CH2, A-CH2CH2-B-CH2, CH2-A-CH2CH2-B, (CH2)3-A-CH2-CH2, etc.; A,

= O, S, S(O), S(O)2; U = aryl, heteroaryl; T = CONR1, (CH2)pOCO, (CH2)pN(R1)CO, (CH2)pN(R1)SO2, CO2; Q = lower alkylene or alkenylene; H = aryl-O(CH2)vR7, heteroaryl-O(CH2)vR7, aryl-O(CH2)vC(CH2)vR7, heteroaryl-(CH2)vG(CH2)wR7, etc.; L = R3, COR3, COR3, CONR2R3, SO2R3, SO2R3, SO2R3, COCR4, COR4, COR4, SO2R3, SO2R3, SO2R3, COCR4, COR4, COR4, SO2R3, SO2R3, SO2R3, SO2R3, SO2R3, SO2R3, COCR4, SO2R3, SO

t, v = 1-4; r = 3-6; s = 2-5; u = 1-3, w = 1,2 integer) and optically .

enantiomers, their mixts. pharmaceutically acceptable salts, solvent complexes, and morphol. forms. These compds. are renin inhibitors and useful for the treatment or prophylaxis of disorders which are assocd. with dysregulation of the renin-angiotensin system (RAS). The disorders include cardiovascular and renal diseases hypertension, congestive heart failure, pulmonary hypertension, cardiac insufficiency, renal insufficiency, renal or myocardial ischemia, atherosclerosis, renal failure, erectile dysfunction, glomerulonephritis, renal colic, glaucoma, diabetic complications, complications after vascular or cardiac surgery, restenosis, complications of treatment with immunosuppressive agents

organ transplantation, and other diseases known to be related to the RAS. For example, 7-[4-[3-[2-chloro-3,6-difluorophenoxy)propyl]phenyl]-3,9-diazabicyclo[3,3.1]non-6-ene-6-carboxylic acid N-cyclopropyl-N-[[2-(2-methoxyethoxy)-3-methylypridin-4-yl]methyl]amide and -[3-(2-Chloro-3,6-difluorophenoxy)propyl]phenyl]-3,9-diazabicyclo[3,3.1]non-6-ene-6-carboxylic acid N-cyclopropyl-N-[3-(2-methoxyethoxy)-2-methylbenzyl]amide showed ICSO of 1.00 and 1.05 nM, resp., against human recombinant renin. 854052-99-6P 854053-00-2P RL: PRC (Pharmacological activity); SFN (Synthetic preparation); THU (Therapeutic use): BIOL (Biological study); PREP (Preparation); USES (Uses) . (preparation of diazabicyclononene derivs. as renin inhibitors for

(preparation of diazabicyclonomene derivs. as renim inhibitors for treatment

tment
 or prophylaxis of disorders associated with dysregulation of
 renin-angiotensin system)
85052-99-6 CAPLUS
3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide, 7-[4-[3-(2-chloro-3,6difluorophenoxy]propyl]phenyl]-N-cyclopropyl-N-[[2-(2-methoxyethoxy)-3methyl-4-pyridinyl]methyl]- (9CI) (CA INDEX NAME)

L4 ANSWER 11 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:
DOCUMENT NUMBER: 142:463754
PITTLE: 142:463754
Preparation of diazabicyclononene derivatives as inhibitors of renin Bezencon, Olivler; Sifferlen, Thierry; Bur, Daniel; Fischli, Walter; Weller, Thomas; Remen, Lubos; Richard-Blidstein, Sylvia Actelion Pharmaceuticals Ltd., Switz.
POT Int. Appl., 37 pp.
COODE: PIXXD2
DOCUMENT TYPE: POT THE Appl., 37 pp.
COODE: PIXXD2
PATENT ANSWER LD.
FAMILY ACC. NUM. COUNT: PIXED2
PATENT INFORMATION: 1

FAMILY ACC. NUM. COUNT: PATENT INFORMATION:

| | PATENT | NO. | | KIN | | | | | | | | | | | | |
|----|------------|---------------------------|-----|-----|-----|------|------|-----|------|------|------|------|-----|-----|------|-----|
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| | W: | AE, AG, | AL, | AM, | AT, | AU, | AZ, | BA, | BB, | BG, | BR, | BW, | BY, | BZ, | CA, | CH, |
| | | CN, CO, | CR, | CU, | CZ. | DE, | DK, | DM. | DZ, | EC, | EE, | EG. | ES. | FI. | GB. | GD. |
| | | GE, GH, | | | | | | | | | | | | | | |
| | | LK, LR, | | | | | | | | | | | | | | |
| | | NO, NZ, | | | | | | | | | | | | | | |
| | | TJ, TM, | | | | | | | | | | | | | | |
| | DW - | BW, GH, | | | | | | | | | | | | | | |
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| | | EE, ES, | | | | | | | | | | | | | | |
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| | | SN, TD, | TG | | | | | | | | | | | | | |
| | | 283821 | | | | | | | | | | | | | | |
| | CA 2540 | 782 | | Al | | 2005 | 0506 | | CA 2 | 004- | 2540 | 782 | | 2 | 0041 | 007 |
| | EP 1678 | 176 | | A1 | | 2006 | 0712 | | EP 2 | 004- | 7901 | 63 | | 2 | 0041 | 007 |
| | R: | AT, BE, | CH, | DE, | DK, | ES, | FR, | GB, | GR, | IT, | LI, | LU, | NL, | SE, | MC, | PT, |
| | | IE, SI, | FI, | RO, | CY, | TR, | BG, | cz, | EE, | HU, | PL, | sĸ | | | | |
| | CN 1867 | 568 | | A | | 2006 | 1122 | | CN 2 | 004- | 8002 | 9967 | | 2 | 0041 | 007 |
| | JP 2007 | 568
508262
50801640 | | T | | 2007 | 0405 | | JP 2 | 006- | 5301 | 10 | | 2 | 0041 | 007 |
| | IN 2006 | CN01640 | | A | | 2007 | 0608 | | TN 2 | 006- | CN16 | 40 | | 2 | 0060 | 511 |
| PR | IORITY APE | LN. INFO | . : | | | | | | WO 2 | 003- | EP11 | 316 | | A 2 | 0031 | 013 |
| | | | | | • | | | | | | | | | | | |
| | | | | | | | | | WO 2 | 003- | EP31 | 1316 | | A 2 | 0031 | 013 |
| | | | | | | | | | | | | | | | | |
| | | | | | | | | | WO 2 | 004- | EP11 | 186 | 1 | W 2 | 0041 | 007 |
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OTHER SOURCE(S): MARPAT 142:463754

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

Title compds. I [X and W independently = N, -CH-; V = -A, -CH2-CH2-CH2-CH2-CH2-CH2-CH2-A-CH2-, etc.; A = 0, S, -So-, etc.; U = ay1, heteroary); T = -cONR1, -CO-, -(CH2)pN(R)1CO-, etc.; R1

H, alkyl, alkenyl, etc.; Q = alkylene, alkenylene; M = aryl-O(CH2)qR2, heteroaryl-O(CH2)qR2, aryl-O(CH2)2O(CH2)yR2, etc.; p = 1-4; R2 = OH, CN, SO3H, etc.; L = -1(CH2)mNN1(CH2)m-1x; X1 = R3, COR3, COOR3, etc.; R3 = H, cycloalkyl, aryl, etc.; q = 2-4; y = 1-2; n and m = 0-1; x = 0-1 with provisions) and their pharmaceutically acceptable salts, are prepared and

L4 ANSWER 11 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN (Continued) disclosed as renin inhibitors. Thus, e.g., II was prepd. by amidation of 2-chloroisonicotinoyl chloride with aniline followed by a methylpyridine2-chloro-3-methylpyridine4-carbaldehyde (III). III underwent reductive amination with cyclopropylamine followed by substitution with 3-(tert-butyldimethylsilanyloxy)propan-1-ol to provide the desired pyridinylmethylamine intermediate which was used to couple with (rac.)-(IR,58)-7-(4-[3-(2-chloro-3,6-difluorophenoxy)propyl)phenyl]3,9-diazabicyclo[3.3.1]non-6-ene-3,6,9-tricarboxylic acid 3,9-di-tert-Bu ester

(prepn. given). The coupling product was subjected to deprotection to provide II. The activity of I was evaluated in in vitro inhibition assays

provide II. The activity of I was evaluated in in vitro inhibition by of human recombinant renin and it revealed that all compds. of the invention possessed ICSO values in the range of 0.49 up to 1.43 nM. I as inhibitors of renin should prove useful in the treatment of diseases such as, but not limited to, hypertension, congestive heart failure and pulmonary hypertension. Pharmaceutical compns. comprising of I are disclosed.

851449-69-9P 851449-70-2P 851449-71-3P
851449-72-4P
RL: PRC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of disracyclonomene derivs. as inhibitors of renin)
851449-69-9 CAPULS
3,9-Diarabicyclo[3,3,1]non-6-ene-6-carboxamide, 7-[4-[3-(2-chloro-3,6-difluorophenoxy)propyl]phenyl]-N-cyclopropyl-N-[[2-(3-hydroxypropoxy)-3-methyl-4-pyridinyl]methyl]- (GCI INDEX NAME)

RN 851449-70-2 CAPLUS
CN 3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide,
N-cyclopropyl-7-[4-[2-(2,6-

dichloro-4-methylphenoxy)ethoxy]phenyl]-N-[{2-(3-hydroxypropoxy)-3-methyl-4-pyridinyl]methyl]- (9CI) (CA INDEX NAME)

L4 ANSWER 11 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN

REFERENCE COUNT:

THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L4 ANSWER 11 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN

851449-71-3 CAPLUS
3,9-Diazabicyclo(3.3.1)non-6-ene-6-carboxamide, 7-[4-{3-(2-chloro-3,6-difluorophenoxy)propyl)phenyl]-M-cyclopropyl-M-[[2-(2-hydroxyethoxy)-3-methyl-4-pyridinyl]methyl]- (9CI) (CA INDEX NAME)

RN 851449-72-4 CAPLUS CN 3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide, N-cyclopropyl-7-[4-[2-(2,6-

dichloro-4-methylphenoxy)ethoxy]phenyl]-N-[{2-(2-hydroxyethoxy)-3-methyl-4-pyridinyl]methyl]- (9CI) (CA INDEX NAME)

L4 ANSWER 12 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:
DOCUMENT NUMBER:
142:38278
Preparation of 3,9-diazabicyclo[3.3.1]nonene derivatives as inhibitors of parasite aspartic proteases
INVENTOR(S):
Bur, Daniel; Fischli, Welter; Remen, Lubos; Richard-Bildstein, Sylvis; Weller, Thomas; Boss, Christoph Binkert, Christoph Meyer, Solange Actelion Pharmaceuticals Ltd., Switz.
PATENT TYPE:
DOCUMENT TYPE:
LANGUAGE:
FAMILY ACC. NUM. COUNT:
FAMILY ACC. NUM. COUNT:
PATENT INFORMATION:

FAMILY ACC. NUM. COUNT: PATENT INFORMATION:

| PAT | PATENT NO. | | | | | D | DATE | | | APPL | ICAT | ION | NO. | | D | ATE | |
|----------|------------|-----|------|-----|-----|-----|------|------|-----|------|------|------|-----|-----|-----|------|-----|
| wo | 2004 | | | | A1 | - | 2004 | 1209 | , | WO 2 | 004- | EP50 | 65 | | 2 | 0040 | 512 |
| | W: | AE, | AG, | AL, | AM. | AT, | AU, | AZ, | BA, | BB, | BG, | BR. | BW. | BY. | BZ. | CA. | CH. |
| | | | | | | | DE, | | | | | | | | | | |
| | | GE, | GH, | GM, | HR, | HU, | ID, | IL, | IN, | IS, | JP, | KE, | KG, | KP, | KR, | KZ. | LC. |
| | | LK, | LR, | LS, | LT, | LU, | LV, | MA, | MD, | MG, | MK, | MN, | MW, | MX, | MZ, | NA, | NI, |
| | | NO, | NZ, | OM, | PG, | PH, | PL, | PT, | RO, | RU, | SC, | SD, | SE, | SG, | SK, | SL, | SY, |
| | | TJ, | TM, | TN, | TR, | TT, | TZ, | UA, | UG, | US, | UZ, | VC, | VN, | YU, | ZA, | ZM, | ZW |
| | RW: | BW, | GH, | GM, | ΚE, | LS, | MW, | MZ, | NA, | SD, | SL, | SZ, | TZ, | UG, | ZM, | ZW, | AM, |
| | | ΑZ, | BY, | KG, | ΚZ, | MD, | RU, | TJ, | TM, | AT, | BE, | BG, | CH, | CY, | CZ, | DE, | DK, |
| | | EE, | ES, | FI, | FR, | GB, | GR, | HU, | IE, | IT, | LU, | MC, | NL, | PL, | PT, | RO, | SE, |
| | | SI, | SK, | TR, | BF, | ВJ, | CF, | CG, | CI, | CM, | GΑ, | GN, | GQ, | GW, | ML, | MR, | NE, |
| | | 5N, | TD, | TG | | | | | | | | | | | | | |
| PRIORITY | APP | LN. | INFO | . : | | | | | 1 | WO 2 | 003- | EP56 | 61 | - 4 | A 2 | 0030 | 530 |

OTHER SOURCE(S): MARPAT 142:38278

Pharmaceutical compns. for treating diseases demanding the inhibition of parasite aspartic proteases contain one or more compound(s) of the cal

parasite aspartic proteases contain one or more compound(s) of the real formula (I) [X, W = N, CH; V = (CH2)r, A-(CH2)s, CH2-A-(CH2)t, (CH2)s-A, (CH2)cA-(CH2)u-R, A(CH2)v-B, (CH2)3-A-CH2, A-CH2CH2-B-CH2, (CH2)3-A-CH2CH2-B-CH2, (CH2)3-A-CH2CH2-B-CH2, CH2-A-CH2CH2-B-CH2, (CH2)3-B-CH2-CH2, CH2-A-CH2CH2-B-CH2, CH2-A-(CH2)3-B, CH2CH2-A-CH2CH2-B (wherein A, B = 0, s, SO, SO2; r = 3-6; s = 2-5; t = 1-4; u = 1-3; v = 2-4; U = aryt, heteroaryt; T = CONR1, (CH2)DCCO, (CH2)DR(R1)CO, (CH2)DR(R1)SO2, COO (wherein R1 = H, lower alkyl, alkenyl, or alkynyl, etc.; p = 1-4); Q = lower alkylene or alkenylene; M = H, cycloalkyl, aryt, heteroaryt; L = R3, COR3, COOR3, COOR3, SOOR3, SOORR3, SOZRR3, SOZRZR3, SOZRR3, SOZRR3, SOZRZR3, SOZRR3, SOZRZR3, SOZRZR3, SOZRZR3, SOZ

racemates, and the meso-form as well as pharmaceutical, solvent complexes and morphol. forms and suitable carrier materials. The pharmaceutical compns. are useful for the treatment or prevention of malaria or diseases caused by protocoal infection. The invention also concerns related aspects including processes for the preparation of the pharmaceutical compns. containing one or more of those compds. and especially their use as inhibitors of plasmepsin II. For example, compound (II) showed IC50

of <10 nM against plasmepsin II.

ANSWER 12 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

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CH-OH

625419-28-5P 625419-30-9P 625419-36-5P 625419-52-5P 625419-99-0P 625420-01-1P 625420-07-1P 625420-31-7P 625420-37-3P 625420-41-9P 625420-41-9P 625420-41-9P 625420-41-9P 625420-41-9P 625420-41-9P 625420-41-9P 625421-42-3P 625421-42-3P 625421-43-6P 625421-60-6P 625421-60-6P 625421-60-6P 625421-60-P 625421-60-P 625421-60-P 625421-60-P 625421-60-P 625421-92-5P 625421-92-5P 625421-92-5P 625421-92-6P 625421-92-P 625431-92-P 625431-92-P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU

ANSWER 12 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN (Continued) 807616-55-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of 3,9-diazabicyclo[3.3.1]nonene derivs. as inhibitors of parasite aspartic proteases)
807616-55-3 CAPLUS
3,9-Diazabicyclo[3.3.1]non-6-ene-3-carboxylic acid, 6-{{{(c-chlorophenyl)methyl|cyclopropylamino|carbonyl]-7-{4-{3-(2,3,6-trifluorophenoxy)propyl]phenyl}-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME 1

625424-37-5P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
(Uses)

(Uses)
(preparation of 3,9-diazabicyclo[3.3.1]nonene derivs. as inhibitors of parasite aspartic proteases)
625424-37-5 CAPLUS
3,9-Diazabicyclo[3.3.1]non-6-ene-3-pentanoic acid, 7-[4-[3-(2-bromo-5-fluorophenoxy)propyl]phenyl]-6-[[cyclopropyl[2-(2,3-difluorophenyl)ethyl]amino]carbonyl]-8-oxo-, monoformate.(9CI) (CA INDEX NAME)

CM 1

CRN 625424-36-4 CMF C39 H41 Br F3 N3 O5

ANSWER 12 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN (Continued) (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of 3,9-diazabicyclo[3,3,1]nonene derivs. as inhibitors of parasite aspartic proteases for treatment or prepn. of malaria diseases.

ases caused by protozoal infection)
625419-28-5 CAPLUS
3,9-Diazabicyclo[3,3.1]non-6-ene-6-carboxamide, 3-acetyl-7-[4-[2-(3-methoxyphenoxy)ethyl]phenyl]-N-methyl-N-(2-phenylethyl)- (9CI) (CA
NAME) (CA INDEX

625419-30-9 CAPLUS
3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide, 3-acetyl-N-methyl-N-(2-phenylethyl)-7-[4-[2-[3-(trifluoromethoxy)phenoxy]ethyl]phenyl]- (9CI)
(CA INDEX NAME)

625419-36-5 CAPLUS
3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide, 3-acetyl-7-{4-{3-{2-chlorophenoxy}propyl]phenyl}-N-methyl-N-{2-phenylethyl}- (9CI) (CA INDEX NAME)

625419-52-5 CAPLUS
3,9-Dlazabicyclo[3.3.1]non-6-ene-6-carboxamide, 3-acetyl-7-[4-[2-(3-bcromophenoxy)ethyl]phenyl]-N-methyl-N-[2-phenylethyl]- (9CI) (CA INDEX

RN 625419-99-0 CAPLUS
CN 3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide,
3-acetyl-M-methyl-7-[4-[2[2-(1-methylethyl)phenoxy]ethyl]phenyl]-N-[2-phenylethyl]- (9CI) (CA INDEX NAME)

RN 625420-01-1 CAPLUS
CN 3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide, 3-acetyl-7-[4-[2-[2-(1,1-dimethylethyl)phenoxy]ethyl]phenyl]-N-methyl-N-(2-phenylethyl)- (9CI)

(CA INDEX NAME)

RN 625420-07-7 CAPLUS

N 3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide, 3-acetyl-7-[4-[2-[2-[1,1-dimethylethyl]]-4-methylphenoxy]ethyl]phenyl]-N-methyl-N-[2-phenylethyl]-(9CI) (CA INDEX NAME)

L4 ANSWER 12 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 625420-49-7 CAPLUS
CN 3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide, 3-acetyl-7-[4-[2-(3,5-dichlorophenoxy)ethyl]phenyl]-N-methyl-N-(2-phenylethyl)- (9CI) (CA INDEX
NAME!

C-N-CH₂-CH₂-Ph C1

RN 625420-91-9 CAPLUS
CN 3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide, 3-acetyl-7-[4-[3-[2-chlorophenoxy]propyl]phenyl]-N-[2-(2-chlorophenyl]ethyl]-N-methyl- (9CI) (CA INDEX NAME)

AC N CH2- CH2 (CH2) 3-0

RN 625420-95-3 CAPLUS
CN 3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide, 3-acetyl-7-[4-{3-{2-chlorophenoxyl peropyl jhenyl}-N-[(2-chlorophenyl)]methyl]-N-cyclopropyl-(9CI) (CA INDEX NAME).

L4 ANSWER 12 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN (Continued

RN 625420-31-7 CAPLUS
3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide, 3-acetyl-7-[4-[2-[2,5-dichlorophenoxy]ethyl]phenyl]-N-methyl-N-[2-phenylethyl]- [9CI] [CA INDEX
NAME]

RN 625420-37-3 CAPLUS
CN 3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide, 3-acetyl-7-[4-[2-(3-chlorophenoxy)ethyl]phenyl]-N-methyl-N-{2-phenylethyl}- (9CI) (CA INDEX NAME)

RN 625420-41-9 CAPLUS
3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide, 3-acetyl-7-[4-(2-[4-(1,1-dimethylethyl])-2-methylphenoxy]ethyl]phenyl]-N-methyl-N-(2-phenylethyl)-(9CI) (CA INDEX NAME)

L4 ANSWER 12 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN (Continued

RN 625420-97-5 CAPLUS
CN 3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide, 3-acetyl-7-[4-[3-(2-chlorophenoxy)propyl]phenyl]-N-methyl-N-(3-phenylbutyl)- [9CI) (CA INDEX NAME)

RN 625421-23-0 CAPLUS
CN 3,9-Dlazablcyclo[3.3.1]non-6-ene-6-carboxamide,
3-acctyl-7-(4-13-(2-bromo5-fluorophenoxy)propyl)phenyl]-N-cyclopropyl-N-(phenylmethyl)- (9CI) (CAINDEX NAME)

AC N CH2 Ph

Ac N CH2)3-0

RN 625421-40-1 CAPLUS
CN 3,9-blazabicyclo[3,3,1]non-6-ene-6-carboxamide,
3-acctyl-7-(4-13-(2-bromo5-fluorophenoxy)propyl]phenyl)-N-[2-(2-chlorophenyl)ethyl]-N-cyclopropyl(9C1) (CA INDEX NAME)

RN 625421-42-3 CAPLUS
CN 3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide,
3-acetyl-7-[4-[3-(2-bromo-5-fluorophenoxy]propyl]phenyl]-N-cyclopropyl-N-[2-(2,3-difluorophenyl)ethyl]- (9CI) (CA INDEX NAME)

RN 625421-44-5 CAPLUS
CN 3,9-Diazabicyclo[3,3.1]non-6-ene-6-carboxamide,
3-acetyl-7-[4-[3-{2-bromo-5-fluorophensyl}propyl]phenyl]-N-cyclopropyl-N-[2-{4-fluorophenyl}ethyl]-(9CI) (CA INDEX NAME)

L4 ANSWER 12 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 625424-22-8 CAPLUS

3,9-Diazabicyclo[3.3.1]non-6-ene-3-pentanoic acid, 7-[4-[3-(2-bromo-5-fluorophenoxy)propyl]phenyl]-6-[[cyclopropyl[(3-(trifluoromethyl)phenyl]methyl]amino]carbonyl]-8-oxo-(9CI) (CA INDEX NAME)

RN 625424-34-2 CAPLUS

S,9-Diazabicyclo[3,3,1]non-6-ene-3-pentanoic acid, 7-[4-[3-(2-bromo-5-fluorophenoxy)propyl]phenyl]-6-[[[2-(2-chlorophenyl)ethyl]cyclopropylamino [carbonyl]-6-oxo- (9CI) (CA INDEX NAME)

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RN 625421-46-7 CAPLUS
CN 3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide,
3-acetyl-7-[4-[3-{Z-bromo-5-fulorophenoxylpropyl]phenyl]-N-cyclopropyl-N-[2-{Z-methylphenyl}ethyl]-(9CI) (CA INDEX NAME)

RN 625421-50-3 CAPLUS
CN 3,9-Diarabicyclo[3.3.1]non-6-ene-6-carboxamide,
3-acetyl-7-(4-(3-(2-bromo-5-fluorophenoxy)propyl]phenyl]-N-cyclopropyl-N-[(3-(trifluoromethyl)phenyl]methyl]- (9CI) (CA INDEX NAME)

L4 ANSWER 12 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 625424-36-4 CAPLUS
CN 3,9-Diazabicyclo[3.3.1]non-6-ene-3-pentanoic acid, 7-[4-(3-(2-bromo-5-fluorophenoxy)]propyl]phenyl]-6-[(cyclopropyl[2-(2,3-difluorophenyl)ethyl]amino]carbonyl]-8-oxo- (9CI) (CA INDEX NAME)

RN 625424-48-8 CAPLUS

S, 9-Diazabicyclo[3.3.1]non-6-ene-3-pentanoic acid, 7-[4-[3-(2-bromo-5-fluorophenoxy]propyl]phenyl]-6-[(cyclopropyl](2-fluorophenyl)methyl]amino]carbonyl]-8-oxo-, methyl ester [9CI] (CA INDEX NAME)

625424-50-2 CAPLUS
3,9-Diazabicyclo[3.3.1]non-6-ene-3-pentanoic acid, 7-[4-[3-(2-bromo-5-fluorophenoxy)propyl]phenyl]-6-[[cyclopropyl[[3-(trifluoromethyl]phenyl]methyl]amino]carbonyl]-8-oxo-, methyl ester (9CI) (CA INDEX NAME)

625424-52-4 CAPLUS
3,9-Diazabicyclo[3.3.1]non-6-ene-3-pentanoic acid, 7-[4-[3-(2-bromo-5-fluorophenoxy)propyl]phenyl]-6-[[cyclopropyl[(2-methylphenyl)methyl]henyl)methyl]henyl)methyl]henyl)methyl]henyl)methyl]henyl)methyl]henyl)methyl]henyl)methyllhenyl)methyllhenyl)methyllhenyl)methyllhenyl)methyllhenyl)methyllhenyl)methyllhenyl)methyllhenyl)methyllhenyl)methyllhenyl

L4 ANSWER 12 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN

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625424-64-8 CAPLUS
3,9-Diazabicyclo[3.3.1]non-6-ene-3-pentanoic acid, 7-{4-[3-(2-bromo-5-fluorophenoxy)propyl]phenyl]-6-[[cyclopropyl[2-{2,3-difluorophenyl}ethyl]amino]carbonyl]-8-oxo-, methyl ester (9CI) (CA INDEX NAME)

625424-66-0 CAPLUS
3,9-Diazabicyclo[3.3.1]non-6-ene-3-pentanoic acid, 7-[4-[3-(2-bromo-5-flucrophenoxy)propyl]phenyl]-6-[[cyclopropyl[2-(4-flucropheny])ethyl]amino]carbonyl]-8-oxo-, methyl ester (9CI) (CA INDEX NAME)

625424-68-2 CAPLUS
3,9-Dlazabicyclo[3.3.1]non-6-ene-3-pentanolc acid, 7-[4-[3-(2-bromo-5-fluorophenoxy)propyl)phenyl]-6-[[cyclopropyl[2-(2-methylphenyl]ethyl]amino]carbonyl)-6-oxo-, methyl ester (9CI) (CA INDEX NAME)

625424-60-4 CAPLUS
3,9-Diazabicyclo[3.3.1]non-6-ene-3-pentanoic acid, 7-[4-[3-(2-bromo-5fluorophenoxy)propyl]phenyl]-6-[[cyclopropyl(2-phenylethyl)amino]carbonyl]-8-oxo-, methyl ester (9CI) (CA INDEX NAME)

625424-62-6 CAPLUS 3,9-Diazabicyclo[3.3.1]non-6-ene-3-pentanoic acid, 7-[4-[3-(2-bromo-5-

ANSWER 12 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

625424-70-6 CAPLUS
3,9-Dlazabicyclo[3.3.1]non-6-ene-3-pentanoic acid, 7-[4-[3-(2-bromo-5-fluorophenoxy)propyl]phenyl]-6-[[cyclopropyl[(3,5-dimethoxyphenyl]methyl]amino]carbonyl]-8-oxo-, methyl ester (9CI) (CA INDEX NAME)

625424-72-8 CAPLUS
3,9-Diazabicyclo[3.3.1]non-6-ene-3-pentanoic acid, 7-[4-(3-(2-bromo-5-fluorophenoxy)propyl]phenyl]-6-[[cyclopropyl[2-(4-methylphenyl]ethyl]amino]carbonyl]-8-oxo-, methyl ester (9CI) (CA INDEX NAME)

RN 625426-50-8 CAPLUS
CN 3,9-Diazabicyclo[3.3.1]non-6-ene-3-pentanoic acid, 7-[4-[3-(2-bromo-5-fluorophenoxy)propyl]phenyl]-6-[[((2-chlorophenyl)methyl]cyclopropylamino]
carbonyl]-8-oxo-, methyl ester (9CI) (CR INDEX NAME)

RN 625426-61-1 CAPLUS
3,9-Diazabicyclo[3.3.1]non-6-ene-3-pentanoic acid, 7-[4-[3-(2-bromo-5-fluorophenoxy)propyl]phenyl]-6-[[cyclopropyl[phenylmethyl]amino]carbonyl]-6-xo-, methyl ester (9c1) (CA INDEX NAME)

L4 ANSWER 12 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 625427-92-1 CAPLUS

3,9-Diazabicyclo[3,3.1]non-6-ene-3-pentanoic acid, 7-[4-[2-(2-chloro-4,5-dimethylphenoxylyethoxylphenyl]-6-[[cyclopropyl[[3-(trifluoromethyl)phenyl]methyl]amino]carbonyl]-8-oxo-, methyl ester

[SCI (CA INDEX NAME)

RN 625431-53-0 CAPLUS

CN 3,9-Dlazablcyclo[3.3.1]non-6-ene-6-carboxamide, 3-acetyl-7-[4-[3-{2-chlorophenoxy}]propyl]phenyl]-N-[{2-chlorophenyl}methyl]-N-methyl- (9CI)
(CA INDEX NAME)

L4 ANSWER 12 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN

RN 625427-38-5 CAPLUS
CN 3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide, 7-{4-[2-[2-chloro-4,5-dimethylphenoxy]ethoxy]phenyl]-N-[(2-chlorophenyl)methyl]-N-ethyl-3-formyl-(GI INDEX NAME)

RN 625427-86-3 CAPLUS

N 3,9-Diazabicyclo[3.3.1]non-6-ene-3-pentanoic acid, 7-[4-[2-(2-chloro-4,5-dimethyl)phenoxy]ethoxy]phenyl]-6-[[[(2-chlorophenyl)methyl]cyclopropylamin o|carbonyl]-8-oxo-, methyl ester (9CI) (CA INDEX NAME)

RN 625427-88-5 CAPLUS

N 3,9-Diazabicyclo[3.3.1]non-6-ene-3-pentanoic acid, 7-{4-[2-(2-chloro-4,5-dimethyl)penoxy]phenyl]-6-[[[(2-chlorophenyl)methyl]ethylamino]carbonyl]-6-oxo-, methyl eater (9CI) (CA INDEX NAME)

L4 ANSWER 12 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 625433-91-2 CAPLUS
CN 3,9-Diazabicyclo[3.3.1]non-6-ene-3-pentanoic acid, 7-[4-[2-(2-bromo-5-fluorophenoxy) ethyl]phenyl]-6-[[methyl(2-phenylethyl)amino]carbonyl]8-oxo- (9CI) (CA INDEX NAME)

RN 807615-51-6 CAPLUS

3,9-Diazabicyclo[3,3.1]non-6-ene-3-pentanoic acid, 7-[4-[3-(2-bromo-5-fluorophenoxy)propyl]phenyl]-6-[[cyclopropyl[phenylmethyl]amino]carbonyl]-α,α-dimethyl-8-oxo- [9CI] (CA INDEX NAME)

RN 807615-53-8 CAPLUS
SN 3,9-Diazabicycio[3,3,1]non-6-ene-3-pentanoic acid, 7-[4-[3-(2-bromo-5-fluorophenoxy) propyl] phenyl]-6-[(cyclopropyl] (2-methylphenyl) methyl] mino[carbonyl]-α,α-dimethyl-8-oxo-(9CI)
(GCI) (CA INDEX RAME)

RN 807615-57-2 CAPLUS
CN 3,9-Diazabicyclo[3.3.1]non-6-ene-3-pentanoic acid, 7-[4-[3-(2-bromo-5-

fluorophenoxy)propyl]phenyl]-6-[[[(2-chlorophenyl)methyl]cyclopropylamino] carbonyl]-a,a-dimethyl-8-oxo- (9CI) (CA INDEX NAME)

RN 807615-60-7 CAPLUS
CN 3,9-Diazabicyclo[3.3.1]non-6-ene-3-pentanoic acid, 7-[4-[3-(2-bromo-5-fluorophenoxy]propyl]phenyl]-6-[[cyclopropyl[(3-(trifluoromethyl)phenyl]methyl]amino]carbonyl]-a,a-dimethyl-8-oxo- (9CI) (CA INDEX NAME)

L4 ANSWER 12 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 807615-70-9 CAPLUS
3,9-Diazabicyclo[3.3.1]non-6-ene-3-pentanoic acid, 6-[[(2-chlorophenyl)michtyl]-α,α-dimethyl-8-oxo-7-[4-[3-(2,4,6-trifluorophenoxy)propyl]phenyl]- (9CI) (CA INDEX NAME)

RN 807615-71-0 CAPLUS

SN 3,9-Diazabicyclo[3.3.1]non-6-ene-3-pentanoic acid, 6-[[cyclopropyl[[3-(trifluoromethyl)phenyl]methyl]amino]carbonyl]-8-oxo-7-[4-[3-(2,4,6-trifluorophenoxy)propyl]phenyl]-, methyl ester (9CI) (CA INDEX NAME)

He HO₂C-C-CH₂-

RN 807615-62-9 CAPLUS
3,9-Diazabicyclo[3,3.1]non-6-ene-6-carboxamide, 7-[4-[3-(2-bromo-5-fluorophenoxy]propyl]phenyl]-N-cyclopropyl-3-[(2R,48)-4-hydroxy-2-pyrrolidinyl]carbonyl]-N-[[3-(trifluoromethyl)phenyl]methyl]- (9CI)
INDEX NAME)

Absolute stereochemistry.

RN 80.7615-68-5 CAPLUS
3,9-Diazabicyclo(3.3.1)non-6-ene-3-pentanoic acid, 6-[[(2-chloropheny)methyl|cyclopropylamino]carbonyl]-8-oxo-7-[4-[3-(2,4,6-trifluorophenoxy)propyl]phenyl]-, methyl ester (9CI) (CA INDEX NAME)

L4 ANSWER 12 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 807615-72-1 CAPLUS
3,9-Diazabicyclo[3.3.1]non-6-enè-6-carboxamide, 3-acetyl-N-[(2-chloropheny).methyl]-N-cyclopropyl-7-[4-[3-(2,4,6-trifluorophenoxy)propyl)phenyl]- (9CI) (CA INDEX NAME)

RN 807615-73-2 CAPLUS
CN 3,9-Diazabicyclo(3.3.1)non-6-ene-3-pentanoic acid, 6-[[[{2-chlorophenyl}methyl]cyclopropylamino|carbonyl]-8-oxo-7-[4-[3-(2,4,6-trifluorophenoxy)propyl)phenyl]- (9CI) (CA INDEX NAME)

RN 807615-74-3 CAPLUS
CN 3,9-blazabicyclo[3.3.1]non-6-ene-6-carboxamide,
N-[(2-chlorophenyllmethyl]N-cyclopropyl-7-[4-[3-(2,4,6-trifluorophenoxy)propyl]phenyl]- [9CI] (CA INDEX NAME)

807615-75-4 CAPLUS 3,9-Diazabicyclo[3.3.1]non-6-ene-3-pentanoic acid, 7-[4-[2-[4-bromophenoxy]ethoxy]phenyl]-6-[[cyclopropyl[[3-(trifluoromethyl]phenyl]methyl]amino]carbonyl]-a,a-dimethyl-8-oxo-[9C] (CA INDEX NAME)

807615-76-5 CAPLUS
3,9-Diazabicyclo[3.3.1]non-6-ene-3-pentanoic acid, 7-[4-[2-(2-chloro-4,5-dimethylphenoxy) ethoxy]phenyl]-6-[[cyclopropyl[[3-(trifluoromethyl)phenyl]methyl]amino]carbonyl]-a,a-dimethyl-8-oxo-(9C) (CA INDEX NAME)

ANSWER 12 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

807615-80-1 CAPLUS
3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide, N-butyl-7-{4-[3-{2-chlorophenoxy)propyl]phenyl]-3-formyl-N-(phenylmethyl)- (9CI) (CA INDEX NAME)

807615-81-2 CAPLUS
3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide, 7-[4-[3-(2-chlorophenoxy)propyl]phenyl]-N-[3-(2-chlorophenoxy)propyl]-3-formyl-N-methyl- (9CI) (CA INDEX NAME)

807615-82-3 CAPLUS
3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide, 7-[4-[3-(2-chlorophenoxy)propyl]phenyl]-N-[(3,4-difluorophenyl)methyl]-3-formyl-N-methyl- (9CI) (CA INDEX NAME)

L4 ANSWER 12 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

807615-77-6 CAPLUS 3,9-Diazabicyclo{3.3.1}non-6-ene-6-carboxamide, 7-[4-[3-(2-

chlorophenoxy)propyl]phenyl]-N-[2-(4-fluorophenyl)ethyl]-3-formyl-N-methyl-(9CI) (CA INDEX NAME)

807615-78-7 CAPLUS
3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide, 7-[4-{3-{2-chlorophenoxy}propyl]phenyl]-N-[(3,4-dichlorophenyl)methyl]-3-formyl-N-methyl- (9C1) (CA INDEX NAME)

RN 807615-79-8 CAPLUS
CN 3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide,
N-[(4-bromophenyl)methyl]7-[4-[3-(2-chlorophenoxy)propyl]phenyl]-3-formyl-N-methyl- (9CI) (CA INDEX NAME)

ANSWER 12 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

807615-83-4 CAPLUS
3,9-Diazabicyclo(3.3.1]non-6-ene-6-carboxamide, 7-[4-{3-(2-chlorophenoxy)propyl]phenyl]-N-[{2,4-dichlorophenyl}methyl]-3-formyl-N-methyl- (9CI) (CA INDEX NAME)

807615-84-5 CAPLUS 3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide, 7-[4-[3-(2-

chlorophenoxy)propyl]phenyl]-N-{(4-chlorophenyl)methyl}-3-formyl-N-methyl-(9CI) (CA INDEX NAME)

807615-85-6 CAPLUS 3,9-Diazabicyclo{3.3.1}non-6-ene-6-carboxamide, $7-\{4-\{3-\{2-4\}\}\}$

807615-86-7 CAPLUS
3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide, 3-acetyl-7-[4-[3-{2-chlorophenoxy}propyl]phenyl)-N-methyl-N-[{3-methylphenyl}methyl]- (9CI)
(CA INDEX NAME)

807615-87-8 CAPLUS 3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide, 3-acetyl-7-[4-[3-(2-

chlorophenoxy)propyl]phenyl]-N-methyl-N-[[4-(trifluoromethyl)phenyl]methyl
]- (9CI) (CA INDEX NAME)

807615-88-9 CAPLUS 3,9-Diazabicyclo(3.3.1)non-6-ene-6-carboxamide, 3-acetyl-7-[4-[3-[2-chlorophenxy]propyl]phenyl]-N-methyl-N-[2-{2-methylphenyl}ethyl]- (9CI) (CA INDEX NAME)

ANSWER 12 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

807615-93-6 CAPLUS
3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide, 3-acetyl-N-[2-{2-bromophenyl}-6thyl]-7-[4-{3-(2-chlorophenoxy)propyl]phenyl]-N-methyl-

(9CI)

(CA INDEX NAME)

807615-94-7 CAPLUS 3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide, 3-acetyl-7-[4-[3-{2-chlorophenoxy)propyl]phenyl]-N-[2-{2,4-difluorophenyl}ethyl]-N-methyl-(9CI) (CA INDEX NAME)

807615-95-8 CAPLUS
3,9-Diazabicyclo(3.3.1]non-6-ene-6-carboxamide, 3-acetyl-7-[4-[3-(2-chlorophenoxy)propyl]phenyl]-N-methyl-N-(5-phenylpentyl)- (9CI) (CA INDEX NAME)

ANSWER 12 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

807615-89-0 CAPLUS 3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide, 3-acetyl-7-[4-[3-{2-chlorophenoxy)propyl]phenyl}-N-[2-(3,4-difluorophenyl)ethyl]-N-methyl-(9CI) (CA INDEX NAME)

807615-90-3 CAPLUS 3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide, 3-acetyl-7-[4-[3-(2-chlorophenoxy)propyl]phenyl]-N-[(3-chlorophenyl)methyl]-N-methyl- (9CI) (CA INDEX NAME)

807615-92-5 CAPLUS 3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide, 3-acetyl-7-[4-[3-{2-chlorophenoxy]propyl]phenyl]-N-[(3,4-difluorophenyl)methyl]-N-methyl-(SCI) (CA INDEX NAME)

L4 ANSWER 12 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

807615-96-9 CAPLUS
3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide, 3-acetyl-7-[4-[3-(2-chlorophenoxy)propyl]phenyl]-N-methyl-N-[3-(2-methylphenyl)propyl]- (9CI)
(CA INDEX NAME)

807615-97-0 CAPLUS
3,9-Diazabicyclo(3.3.1]non-6-ene-6-carboxamide, 3-acetyl-7-[4-[3-(2-chlorophenoxy)propyl]phenyl]-N-(2-phenylethyl)-N-(phenylmethyl)- (9CI)
(CA INDEX NAME)

807615-98-1 CAPLUS
3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide, 3-acetyl-7-[4-[3-{2-chlorophenoxy}propyl]phenyl]-N-[2-(2,4-dichlorophenyl)ethyl]-N-methyl-(9CI) (CA INDEX NAME)

RN 807615-99-2 CAPLUS
3, 9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide, 3-acetyl-7-[4-{3-{2-chlorophenoxy)propyl]phenyl]-N-methyl-N-[2-(2,4,6-trimethylphenyl)ethyl](9C1) (CA INDEX NAME)

RN 807616-00-8 CAPLUS
CN 3,9-Diazabicyclo[3.3.1]non-6-ene-3-pentanoic acid, 7-[4-[3-(2-bromo-5-fluorophenoxy)propyl]phenyl]-6-[[cyclopropyl[2-(2,3-difluorophenyl]-ethyl]amino]carbonyl]-α,α-dimethyl-δ-oxo-(9CI) (CA INDEX NAME)

RN 807616-01-9 CAPLUS
CN 3,9-Diazabicyclo[3.3.1]non-6-ene-3-pentanoic acid, 7-[4-[3-(2-bromo-5-

L4 ANSWER 12 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 807616-04-2 CAPLUS
3,9-Diazabicyclo[3.3.1]non-6-ene-3-pentanoic acid, 7-{4-[3-(2-bromo-5-fluorophenoxy]propyl]phenyl]-6-[(cyclopropyl)[2-(4-fluorophenyl)]-thyl]amino]carbonyl]-α,α-dimethyl-δ-οχο-(9CI) (CA INDEX NAME)

RN 807616-05-3 CAPLUS
3,9-Diazabicyclo[3.3.1]non-6-ene-3-pentanoic acid, 7-[4-[3-(2-bromo-5-fluorophenoxy)propyl]ph-ene-flower-flow

L4 ANSWER 12 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

fluorophenoxy)propyl]phenyl]-6-[[(2-(2-chlorophenyl)ethyl]cyclopropylamino]carbonyl]-7,7-dimethyl-8-oxo- (9CI) (CA INDEX NAME)

RN 807616-02-0 CAPLUS

CN 3,9-Dlazabicyclo[3.3.1]non-6-ene-3-pentanoic acid, 7-[4-[3-(2-bromo-5-fluorophenoxy]propyl]phenyl]-6-[[cyclopropyl[2-(2-methylphenyl)ethyl]mino]carbonyl]-y,y-dimethyl-6-oxo-[9CI] (CA INDEX NAME)

RN 807616-03-1 CAPLUS
CN 3,9-Diazabicyclo[3.3.1]non-6-ene-3-pentanoic acid, 7-[4-[3-(2-bromo-5-

fluorophenoxy)propyl]phenyl]-6-[{cyclopropyl(2-phenylethyl)amino}carbonyl}α,α-dimethyl-6-oxo- {9CI} (CA INDEX NAME)

L4 ANSWER 12 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 807616-06-4 CAPLUS
CArbamic acid, [5-(7-[4-[2-(2-bromo-4-fluorophenoxy)ethyl]phenyl]-6[[methyl(2-phenylethyl)amino|carbonyl]-3,9-diazabicyclo[3.3.1]non-6-en-3yl]-1,5-dioxopentyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

PAGE 1-B

RN 807616-07-5 CAPLUS
CN 1-Piperidinecarboxylic acid, 4-[[7-[4-[2-[2-bromo-4-fluorophenoxylethyl]phenyl]-6-[[methyl [2-phenylethyl]amino]carbonyl]-3,9-diazabicyclo[3.3.1]non-6-en-3-yl]carbonyl]-, 1,1-dimethylethyl ester

(9CI)
(CA INDEX NAME)

807616-08-6 CAPLUS .

3,9-Diazabicyclo(3.3.1)non-6-ene-6-carboxamide, 7-{4-{2-(2-bromo-5-floorophenoxy)ethyl)phenyl}-3-(3-hydroxy-1-oxobutyl)-N-methyl-N-{2-phenylethyl}- (9CI) (CA INDEX NAME)

807616-09-7 CAPLUS
3,9-Dlazabicyclo[3.3.1]non-6-ene-6-carboxamide, 7-[4-[2-(2-bromo-5-fluorophenoxy)ethyl]phenyl]-N-methyl-N-(2-phenylethyl)-3-(1H-tetrazol-1-ylacetyl)- (9CI) (CA INDEX NAME)

807616-10-0 CAPLUS
3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide, 7-{4-[2-(2-bromo-5-fluorophenoxy)ethyl]phenyl]-3-(hydroxyacetyl)-N-methyl-N-(2-phenylethyl)-(9CI) (CA INDEX NAME)

L4 ANSWER 13 OF 15
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13 195706
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INVENTOR(S):
BEZENCEN, Olivier, Bur, Daniel; Fischli, Walter;
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| | R: | AT, | BE. | CH. | DE. | DK. | ES. | FR. | GB. | GR. | IT. | LT. | T.U. | NI | SE. | MC. | PT. |
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| ĊN | 1780 | 1836 | | , | Δ, | , | 2006 | 0531 | , | CN 2 | 004- | 8001 | 1240 | | , | 0040 | 426 |
| .10 | 2006 | 55246 | 56 | | T. | | 2006 | 1102 | | TD 2 | 006- | 5052 | 62 | | | 0040 | 426 |
| 119 | 200 | 62173 | 71 | | A1 | | 2006 | 0020 | | 110 2 | 005- | 5544 | 42 | | , | 0051 | 025 |
| CN
JP
US
RIORIT | V ADI | DT.N | TNEO | | ~1 | | 2000 | 0320 | | WO 2 | 003- | ED43 | 93 | | n 2 | 0030 | 428 |
| | | ш. | | • • | | | | | | -0 2 | 003- | DF 43 | ,, | • | | 0030 | 120 |
| | | | | | | | | | | WO 2 | 003- | EP30 | 4393 | | A 2 | 0030 | 428 |
| | | | | | | | | | | | | | | | - | | |
| | | | | | | | | | | WO 2 | 004- | EP43 | 73 | 1 | w 2 | 0040 | 426 |
| | | | | | | | | | | | | | | | | | |

OTHER SOURCE(S): MARPAT 141:395706

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

3,9-Diazabicyclo[3.3.1]nonene derivs. I (Z, Y, X, W = N, or -CH; V = alkyl, alkoxy, sulfide, sulfoxy, sulfate; U = aryl, heteroaryl; T = amide,

e, sulfamide, ester; Q = lower alkylene or alkenylene; L = H, alkyl, alkene, aryl, heteroaryl, alkoxy, aryloxy, CN, ester, amide, sulfate, sulfamide, etc.; M = H, cycloalkyl, aryl, heterocycle, heteroaryl) were prepared a renin inhibitors for the treatment of cardiovascular and renal diseases. Thus, II was treated with 2-chlorophenol, TMAD, and tri-Bu phosphine to give the aryl ather which was deprotected using THC/AcOH to give III.

ANSWER 12 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN

REFERENCE COUNT:

THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L4 ANSWER 13 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

17 790696-38-7P 790696-39-9P 790696-40-1P

790696-41-2P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
(Uses)

[Uses)

[Uses]

inhibitors

for the treatment of cardiovascular disease, renal diseases, and other
related conditions)

RN 790696-38-7 CAPLUS

CN 3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide,
N-cyclopropyl-7-[4-2-(2,6-dichloro-4-methylphenoxy)ethoxy]phenyl]-N-[(3-methoxy-2methylphenyl)methyl]-(SCI) (CA INDEX NAME)

790696-39-8 CAPLUS 3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide, N-cyclopropyl-7-[4-[4-[2-fluor-6-(trifluoromethyl)phenoxy]butoxy]phenyl]-N-[(3-methoxy-2-methylphenyl)methyl]- (9CI) (CA INDEX NAME)

RN 790696-40-1 CAPLUS
CN 3,9-blazabicyclo(3.3.1)non-6-ene-6-carboxamide,
N-cyclopropyl-7-(4-[4-(2,6dichloro-4-methyl)phenoxy)butoxy]phenyl]-N-[(3-methoxy-2methylphenyl)methyl-(9CI) (CA INDEX NAME)

790696-41-2 CAPLUS 79095947-2 Artos 3,9-Diazabicyclo[3,3.1]non-6-ene-6-carboxamide, [4-(2-chloro-6-fluoro-4-methylphenoxy)butoxy]phenyl]-N-cyclopropyl-N-[(3-methoxy-2-methylphenyl)methyl]- [9CI) (CA INDEX NAME)

REFERENCE COUNT:

THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

ANSWER 14 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

The invention relates to novel 3,9-diazabicyclo[3.3.1]nonene derivs. of formula [I] [wherein W = six-membered non benzofused, Ph or heterocyclic ring substituted in the meta or para positions; V = OCHIZCH(ONE)CHO, OCHIZCH(Me)CH2O, OCHIZCH(Me)CH2O, OCHIZCH(Me)CH2O, OCHIZCH(Me)CH2O, OCHIZCH(ME)CO, OCHIZCH(M

heteroaryl; L = R3, COR3, COR3, CONR2R3, SO2R3, SO2RR2R3, COCH(Aryl)2;

R1

= H; lower alkyl, lower alkenyl, lower alkynyl, cycloalkyl, aryl,
cycloalkyl-lower alkyl; R2 = H, lower alkyl, lower alkenyl, cycloalkyl,
cycloalkyl-lower alkyl; R3 = H, lower alkyl, lower alkenyl, cycloalkyl,
aryl, heteroaryl, heterocyclyl, cycloalkyl, arylowy-lower alkyl,
heteroaryl-lower alkyl, heterocyclyl-lower alkyl, arylowy-lower alkyl,
heteroaryl-lower alkyl, where by these groups may be unaubstituted or
mono, di - or trisubstituted; m, n = 0 or 1 with the proviso that in case
m is 1, n is 0, or vice versa; p = an integer of 1-4; k = an integer of
0-11 and optically pure enanticmers, mixts. of enanticmers such as
racemates, diasteroemers, mixts. of diasteroemers, diasteroemeric
racemates, etc. and pharmaceutically acceptable salts, solvates, and
morphol. forms were prepared Also provided are pharmaceutical compns.
containing the compds. as the active ingredients for treatment or
prophylaxis
of disorders which are associated with a dysregulation of the
renin-angiotensin system (RAS), comprising cardiovascular and renal
diseases, hypertension, congestive heart failure, pulmonary hypertension,
cardiac insufficiency, renal insufficiency, renal or myocardial ischemia,
atherosclerosis, renal failure, exectile dysfunction, glomerulomephritis,
renal colic, glaucoma, diabetic complications, complications of treatment with
immunosuppressive agents after organ transplantation, and other diseases
known to be related to the RAS. Thus, (IR, SS)-7-[4-[(2S)-2-methyl-3(2,3,6-trifluorophenoxy)propoxy|phenyl|-3,9-diazabicyclo[3,3,1]non-6-ene-6-

(2,3,6-trifluorophenoxy)propoxy]phenyl)-3,9-diazabicyclo(3.3.1)non-6-ene-6-carboxylic acid cyclopropyl(2,3-dichlorobenzyl)amide and

(1S, SR) -7-{4-{(2S)-2-methyl-3-(2,3,6-trifluorophenoxy)propoxy]phenyl}-3,9-diazabicyclo[3,3.1]non-6-ene-6-carboxylic acid cyclopropyl(2,3-dichlorobenzyl)amide were prepared starting from (-)-Me D-β-hydroxyisobutyrate.
IT 791065-37-7P 793709-22-5P RI: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP

L4 ANSWER 14 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:964985 CAPLUS
DOCUMENT NUMBER: 141:410959
TITLE: Preparation of
7-aryl-3,9-diazabicycl0[3.3:],lonn-6-ene
derivatives and their use as renin inhibitors in the
treatment of hypertension, cardiovascular or renal
LNUMNTOR(S): Recogn. Olivier: Bur. Daniel: Flachli, Walter:

diseases
Bezencon, Olivier; Bur, Daniel; Fischli, Walter;
Remen, Lubos; Richard-Bildstein, Sylvia; Weller,
Thomas; Sifferlen, Thierry
Actelion Pharmaceuticals Ltd., Switz.
PCT Int. Appl., 32 pp.
CODEN: PIXXD2
Patent INVENTOR (S):

PATENT ASSIGNEE(S): SOURCE:

DOCUMENT TYPE: Patent

English LANGUAGE:

FAMILY ACC. NUM. COUNT: PATENT INFORMATION:

| | | TENT | | | | | | DATE | | | | | | | | | | |
|-----|-----|------|------|------|-----|-----|-----|------|------|-----|------|------|------|------|-----|-----|------|-----|
| | | | | | | | | | | | | | | | | | | |
| | WO | 2004 | 0961 | 16 | | A2 | | 2004 | 1111 | 1 | WO 2 | 004- | EP43 | 72 | | 2 | 0040 | 426 |
| | WO | 2004 | 0961 | 16 | | A3 | | 2005 | 0324 | | | | | | | | | |
| | | W: | AE, | AG, | AL, | AM, | AT, | AU, | AZ, | BA, | 88, | BG, | BR, | BW, | BY, | BZ, | CA, | CH. |
| | | | | | | | | | | | | EC, | | | | | | |
| | | | | | | | | | | | | JP, | | | | | | |
| | | | | | | | | | | | | MK, | | | | | | |
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| | | DW. | | | | | | | | | | SL, | | | | | | |
| | | | | | | | | | | | | BE. | | | | | | |
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| | | | | | | | | | | | | LU, | | | | | | |
| | | | | | | BF, | ы, | CF, | CG, | CI, | CM, | GΑ, | GN, | GQ, | GW, | ML, | MK, | NE, |
| | | | | TD, | | | | | | | | | | | | _ | | |
| | | 2004 | | | | | | | | | | | | | | | | |
| | | 2521 | | | | | | | | | | | | | | | | |
| | | 1622 | | | | | | | | | | | | | | | | |
| | • | R: | | | | | | | | | | | | | | SE, | MC, | PT, |
| | | | | | | | | | | | | HU, | | | | | | |
| | BR | 2004 | 0098 | 82 | | A | | 2006 | 0523 | | BR 2 | 004- | 9882 | | | 2 | 0040 | 426 |
| | CN | 1780 | 838 | | | A | | 2006 | 0531 | | CN 2 | 004- | 8001 | 1650 | | 2 | 0040 | 426 |
| | JΡ | 2006 | 5252 | 59 | | T | | 2006 | 1109 | | JP 2 | 006- | 5052 | 61 | • | 2 | 0040 | 426 |
| | US | 2006 | 2237 | 95 | | Al | | 2006 | 1005 | | US 2 | 005- | 5553 | 82 | | 2 | 0051 | 102 |
| RIO | RIT | APP | LN. | INFO | .: | | | | | • | WO 2 | 003- | EP30 | 4622 | | A 2 | 0030 | 502 |
| | | | | | | | | | | | WO 2 | 004- | EP43 | 72 | | w 2 | 0040 | 426 |

OTHER SOURCE(S):

CASREACT 141:410959; MARPAT 141:410959

ANSWER 14 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN (Continued) (Preparation); RACT (Reactant or reagent); USES (Uses) (prepn. of 7-aryl-3,9-diazabicyclo[3,3.1]non-6-ene derivs. and their use as renin inhibitors in treatment of hypertension, cardiovasculer

renal diseases)

791065-37-7 CAPLUS
3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide, N-cyclopropyl-N-[(2,3-dichlorophenyl)methyl]-7-[4-[(28)-2-methyl-3-(2,3,6-trifluorophenoxy)propoxy]phenyl]-, (1R,58)- (9CI) (CA INDEX NAME)

Absolute stereochemistry

793709-22-5 CAPLUS
3,9-Diazabicyclo(3.3.1)non-6-ene-6-carboxamide, M-cyclopropyl-M-{(2,3-dichlorophenyl)methyl]-7-[4-[(28)-2-methyl-3-[2,3,6-trifluorophenoxy)propoxy]phenyl]- (9CI) (CA INDEX NAME)

RI: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (preparation of 7-aryl-3,9-diazabicyclo{3.3.1}non-6-ene derivs. and

use as renin inhibitors in treatment of hypertension, cardiovascular

ANSWER 14 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN (Continued) renal diseases)
791065-38-8 CAPLUS
3,9-Diazabicyclo[3.3.1]non-6-ene-6-carboxamide, N-cyclopropyl-N-{(2,3-dichlorophenyl)methyl)-7-{4-{(2S)-2-methyl-3-(2,3,6-trifluorophenoxy)propoxy]phenyl]-, (1S,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

ANSWER 15 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

The invention relates to novel 3,9-diazabicyclo[3,3,1]nonene derivs. of formula (I) (wherein X, W = N, CH; $V = (CH2)_{Y}$, $A - (CH2)_{S}$

M = H, cycloalkyl, aryl, heterocyciyi, heteroaryi; L = κ3, CURS, CURRS, CORRSA, SOZRRS, SOZRRSA, SOZRRSA, SOZRRSA, SOZRRSA, COCH(Aryll2; R1 = H; lower alkyl, lower alkyl, cycloalkyl, cycloalkyl-lower alkyl, R3 = H, lower alkyl, lower alkenyl, cycloalkyl, cycloalkyl-lower alkyl, R3 = H, lower alkyl, lower alkenyl, cycloalkyl-lower alkyl, heterocyclyl-lower alkyl, etcrocyclyl-lower alkyl, heterocyclyl-lower alkyl, heterocyclycow-lower alkyl, heterocyclycow-lower alkyl, where by these groups may be unsubstituted or mono, di- or vice versa; p, t = an integer of 1-4; r = an integer of 3-6; s = an integer 2-5; u = an integer of 1-4; r = an integer of 3-6; s = an integer 2-5; u = an integer of 1-3; v = an integer of 2-4) and optically pure enantiomers, mixts. of enantiomers such as racemates, diastereomers, mixts. of diastereomers, diastereomeric racemates, diastereomers, mixts. of diastereomers, diastereomeric racemates, diastereomers, injuredients for treatment or prophylaxis of disorders which are associated with a dysregulation of the renin-angiotensin system (RAS), comprising cardiovascular and renal diseases, hypertension, congestive heart fallure, nulmonary hypertension, cardiac insufficiency, renal insufficiency, renal

cardiovascular and tends are related to the failure, pulmonary hypertension, cardiac insufficiency, renal insufficiency, renal or myocardial ischemia, atherosclerosis, renal failure, erectile dysfunction, glomerulonephritis, renal colic, glaucoma, diabetic complications, complications after vascular or cardiac surgery, restenosis, complications of treatment with immunosuppressive agents

organ transplantation, and other diseases known to be related to the RAS. The IC50-values of all compds. tested against recombinant human renin

below 100 nM.
625433-85-4P
RL: PAC (Pharmacological activity); PUR (Purification or recovery); SPN
(Synthetic preparation); THU (Therapeutic use); BIOL (Biological study);
PREP (Preparation); USES (Uses)
(preparation of 7-aryl-3,9-diazabicyclo[3.3.1]non-6-ene derivs. as

inhibitors in the treatment of hypertension, cardiovascular or renal diseases)

L4 ANSWER 15 OF 15 CAPLUS COPYRIGHT 2007 ACS ON STN ACCESSION NUMBER: 2003:892776 CAPLUS DOCUMENT NUMBER: 139:395949

TITLE: Preparation of 7-aryl-3,9-diazabicyclo[3.3.1]non-6-ene

....eir use as renin inhibitors in of hypertension, cardiovascular or ren diseases
Bezencon, Olivier: Bur, Daniel; Fischli, Walter; Remen, Lubos; Richard-Bildstein, Sylvia: Weber, Hans-Peter; Weller; Thomas
Actelion Pharmaceuticals Ltd., Switz.
PCT Int. Appl., 514 pp.
CODEN: PIXXD2
Patent
English derivatives and their use as renin inhibitors in the treatment of hypertension, cardiovascular or renal diseases

Bezencon, Olivier: Bur, Daniel: Flachia

PATENT ASSIGNEE(S): SOURCE:

DOCUMENT TYPE: LANGUAGE: FAMILY ACC. NUM. COUNT: PATENT INFORMATION:

INVENTOR (S):

| PATENT NO. | KIND DAT | E APP | LICATION NO. | DATE |
|------------------------|------------|--------------|---------------|-----------------|
| | | | | |
| WO 2003093267 | A1 200 | 31113 WO | 2003-EP3721 | 20030408 |
| W: AE, AG, AL, | AM, AT, AU | ,—AZ;—BA, BB | , BG, BR, BY, | BZ, CA, CH, CN, |
| CO, CR, CU, | CZ, DE, DK | , DM, DZ, EC | , EE, ES, FI, | GB, GD, GE, GH, |
| GM, HR, HU, | ID, IL, IN | , IS, JP, KE | . KG, KP, KR, | KZ, LC, LK, LR, |
| | | | | NO, NZ, OM, PH, |
| | | | | TN. TR. TT. TZ. |
| | | , YU, ZA, ZM | | |
| RW: GH, GM, KE, | | | | ZW. AM. AZ. BY. |
| | | | | DE, DK, EE, ES, |
| | | | | SE, SI, SK, TR, |
| | | | | NE, SN, TD, TG |
| | | | | 20030408 |
| AU 2003233963 | | | 2003-233963 | |
| EP 1501830 | | | 2003-727287 | |
| R: AT, BE, CH, | DE. DK. ES | . FR. GB. GR | . IT. LI. LU. | NL. SE. MC. PT. |
| | | | , TR, BG, CZ, | |
| * BR 2003009498 | | | | 20030408 |
| CN_164987.0 | A200 | 50803 CN | 2003-809766 | 20030408 |
| US 2005176700 | | | 2003-513103 | |
| JP-2005527602 | | | 2004-501406 | 20030408 |
| NZ 536750 | A 200 | 70223 NZ | 2003-536750 | 20030408 |
| IN 2004CN02435 | 'A 200 | 70302 IN | 2004-CN2435 | 20041027 |
| | | | 2004-5042 | 20041119 |
| PRIORITY APPLN. INFO.: | • | | 2002-EP4705 | |
| | | . "- | | |
| | | WO | 2003-EP3721 | W 20030408 |

OTHER SOURCE(S):

MARPAT 139:395949

ANSWER 15 OF 15 CAPLUS COPYRIGHT 2007 ACS ON STN (Continued) 625433-85-4 CAPLUS 3,9-Diazsbicyclo[3.3.1]non-6-ene-6-carboxamide, 2-chlorophenyl]methyl]- N-cyclopropyl-3-[[(25,4R)-4-hydroxy-2-pyrrolidinyl]carbonyl]-7-[4-[3-(2,3,6-trifluorophenoxy)propyl]phenyl]-, (15,5R)- (9CI) (CA INDEX NAME)

625418-50-0P 625418-51-1P 625418-52-2P 625418-53-3P 625418-51-1P 625418-55-5P 625418-55-6P 625418-51-7P 625418-55-5P 625418-56-6P 625418-65-7P 625418-56-6P 625418-65-7P 625418-66-8P 625418-66-4P 625418-67-4P 625418-67-9P 625418-71-7P 625418-71-5P 625418-71-2P 625418-71-2P 625418-71-7P 625419-71-7P 62541

(Continued)

ANSWER 15 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
625420-14-6P 625420-15-7P 625420-16-8P
625420-18-0P 625420-19-1P 625420-20-4P
625420-22-6P 625420-24-8P 625420-26-0P
625420-34-0P 625420-36-6P 625420-38-4P
625420-34-0P 625420-36-6P 625420-38-4P
625420-40-8P 625420-48-0P 625420-38-4P
625420-53-5P 625420-53-3P 625420-54-4P
625420-53-5P 625420-53-3P 625420-54-4P
625420-53-P 625420-56-6P 625420-51-3P
625420-53-P 625420-66-6P 625420-61-3P
625420-68-0P 625420-60-2P 625420-61-3P
625420-68-0P 625420-60-0P 625420-61-3P
625420-68-0P 625420-60-0P 625420-61-3P
625420-69-0P 625420-61-0P 625420-61-3P
625420-69-0P 625420-62-8P 625420-61-3P
625420-60-6P 625420-62-8P 625420-61-8P
625420-69-0P 625420-60-8P 625420-89-8P
625420-92-0P 625420-88-4P 625420-90-8P
625420-92-0P 625420-94-2P 625420-95-3P
625420-92-0P 625420-10-7P 625421-00-3P
625421-09-1P 625421-10-5P 625421-10-5P
625421-19-4P 625421-10-5P 625421-10-5P
625421-19-4P 625421-21-6P 625421-10-5P
625421-33-2P 625421-35-4P 625421-31-6P
625421-33-3P 625421-35-6P 625421-31-6P
625421-33-3P 625421-35-6P 625421-31-6P
625421-33-8P 625421-31-6P 625421-31-6P
625421-31-8P 625421-31-8P 625421-34-P
625421-31-P 625421-31-8P 625421-34-P
625421-76-1P 625421-31-8P 625421-35-P
625421-76-1P 625421-31-9P 625421-31-P
625421-32-P 625421-31-9P 625421-31-P
625421-32-P 625421-33-9P 625421-31-P
625421-32-P 625421-33-9P 625421-31-P
625421-32-P 625421-33-9P 625421-33-P
625421-33-P 625421-33-9P 625421-33-P
625421-33-P 625421-33-9P 625421-33-P
625421-33-P 625421-33-9P 625421-93-P
625421-33-P 625421-33-9P 625422-00-6P
625422-91-P 625422-38-P 625422-91-P
625422-91-P 625422-91-P 625422-91-P
625422-91-P 625422-91-P 625422-91-P
625422-91-P 625422-91-P 625422-91-P
62542

(prepn. of 7-aryl-3,9-diazabicyclo[3.3.1]non-6-ene derivs. as renin inhibitors in the treatment of hypertension, cardiovascular or renal

inhibitors in the treatment of hypertension, cardiovascular of renal diseases (25418-50-0 CAPLUS Benzeneacetic acid, 2-methoxy-, [3-[(4-chlorophenyl)acetyl]-7-[4-[3-[(2-methoxyphenyl)methoxyphrophyl)methoxyphrophylmethoxyphrophylmethoxyphrophylmethoxyphrophylmethoxyphrophylmethoxyphrophylmethoxyphrophylmethylme

ANSWER 15 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN

RN 625418-52-2 CAPLUS
CN Benzeneacetic acid, 2-methoxy-,
[7-[4-[3-[(2-methoxyphenyl)methoxy]propoxy
]phenyl]-3-(2-quinoxalinyl)a-12-ponyl)-3, 9-diazabicyclo[3.3.1]non-6-en-6yl]methyl ester (9CI) (CA INDEX NAME)

CRN 625418-52-2 CMF C43 H44 N4 O7

(CH2)3-0

ANSWER 15 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN

625418-51-1 CAPLUS
Benzeneacetic acid, 2-methoxy-, [3-[(4-chlorophenyl)acetyl]-7-[4-[3-[(2-methoxyphenyl)methoxyphenyl)methoxyphenyl]-3,9-diazabicyclo[3.3.1]non-6-en-6-yl]methyl ester, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CRN 625418-50-0 CMF C42 H45 C1 N2 O7

CM 2

CRN 76-05-1 CMF C2 H F3 O2

ANSWER 15 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

CM 2

76-05-1 C2 H F3 O2

RN 625418-54-4 CAPLUS

Senzeneacetic acid, 2-methoxy-,

[7-[4-[3-[(2-methoxyphenyl)methoxy]propoxy]
phenyl]-3-[(phenylmethyl)aulfonyl]-3, 9-diazabicyclo[3.3.1]non-6-en-6-yl]methyl ester (9CI) (CA INDEX NAME)

625418-55-5 CAPLUS
Benzeneacetic acid, 2-methoxy-,
1-[3-[(2-methoxypheny1)methoxy]propoxy
]phenyl]-3-[(phenylmethyl)aulfony1]-3,9-diazabicyclo[3.3.1]non-6-en-6y1]methyl ester, mono(trifluoroacetate) [9CI] (CA INDEX NAME)